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HISTORICAL ASPECTS OF THE DEVELOPMENT OF LIVE VIRUS VACCINE IN POLIOMYELITIS*

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To-day, when scientific genius has extended man's intellectual control far beyond the horizons of this planet, it somehow does not seem quite apropos to discuss an infection which, so far as we know, affects the population of only one of the planets and causes illness in only a very small fraction of this population. However, the Committee of the Philadelphia College of Physicians, who have greatly honoured me as a recipient of the Alvarenga Prize, suggested that I should consider vaccination against poliomyelitis as a likely topic, and, acquiescing to their demands, I have decided to trace the history of the development of live polio vaccine.

" History " is one word in the lexicon of all languages which is subject to constant misinterpretation. Hegel was probably right when he said that we learn from history that men never learn anything from history. And there is Fabre's aphorism: " History records the names of royal bastards, but cannot tell us the origin of wheat." I do not intend to lecture about " royal bastards," but perhaps one should remark, in passing, that the relation between a virus disease and legitimate royal offspring was of great importance to the history of France. The younger son of the Duc de Bourgogne, grandson and heir to the throne of Louis XIV, had the opportunity to become Louis XV because his governess was able to hide him when he had measles, thus saving him from treatment by the royal physicians, whose ministrations had already dispatched to the other world his mother, father, and older brother, all of whom had suffered from the same malady (*Saint-Simon at Versailles*, 1958).

Though I am not qualified to discuss " the origin of wheat," I shall attempt to trace the origin of live poliomyelitis vaccine. In doing so I shall be obliged occasionally to dispel certain myths and make sure that the legends and parables surrounding these myths are not substituted for history. I shall do my best to do justice to historical facts, though I am afraid there are some who stand ready to reinstate the myths which I shall dethrone. The statement of Ludwick Wittgenstein, the eminent twentieth-century philosopher: " Der Philosoph behandelt eine Frage; wie eine Krankheit " (The philosopher's treatment of a question is like the treatment of an illness), will dictate the method of my lecture.

The Dawn

On March 15, 16, and 17, 1951, the then National Foundation for Infantile Paralysis called a round-table conference on immunization against poliomyelitis to be held in Hershey, Pa. During the meeting I was asked by the chairman of one of the sessions, Dr. Paul, whether I had any data to present at that time. I shall now quote verbatim the first few paragraphs of my reply:

" The data I want to acquaint you with represent a summary of clinical trials based on oral feeding of children with TN strain of polio (living virus). Properties of this strain were summarized yesterday.

" The TN strain was used at two cotton-rat passage levels: 1st to 3rd and 32nd to 35th. If later we have more time I will summarize, on the blackboard, experimental data of intracerebral inoculation of animals with pools used for feeding purposes. Twenty children and two adults were fed the TN virus and nine of these received material stemming from the 32nd and 35th cotton-rat passage level. The LD_{50} titre in mice of the inoculum ranged from $10^{-5.1}$ to 10^{-6}. Material used for feeding consisted of 10 ml. of 20% suspension of cotton-rat brain and cord infected with TN strain. In many instances the infectious material was mixed with milk and 5% glucose or chocolate milk, and sometimes it was given on a spoon.

" Stools were collected from individuals who were fed virus on the 4th–6th day, the 7th–9th day, the 17–19th day, and the 20th–23rd day."

In continuation of the report, emphasis is placed on the fact that all of the 18 non-immune subjects who remained symptom-free developed antibodies against type II virus as a result of the feeding. In the same report I mentioned two type II immune individuals, neither of whom excreted the virus after feeding and whose levels of antibodies remained the same. This was the first public disclosure of oral administration of living attenuated poliomyelitis virus to a human being, an event which actually took place on February 27, 1950, when a six-year-old boy who had no antibodies against type II virus was given—by Dr. Jervis, Mr. Norton, and myself—an emulsion which tasted like cod-liver oil and was in reality a suspension of cotton-rat cord and brain tissue which had been infected with approximately three million mouse lethal doses of the TN strain (named after my associate, Mr. Thomas W. Norton, who participated actively in the work on the attenuation of this virus).

This boy was the first human subject, anywhere in the world, to be fed live attenuated poliovirus for immunization purposes. He was subjected to carefully controlled clinical and laboratory observation, which revealed that intestinal infection with the virus had been established, without any signs or symptoms of illness. Blood drawn 15 days after oral administration of the TN strain revealed the appearance of specific neutralizing

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antibodies, but we waited 44 days before feeding another type II non-immune subject. After the uneventful period of clinical observation and the development of antibodies in the presence of the intestinal carrier state, virus of the same strain was administered orally to 18 children, bringing the total number to 20 (Koprowski, 1952). This represented the first successful trial of immunization of man against poliomyelitis. Because of its nature, knowledge of this trial was at first confined to Dr. Jervis, Mr. Norton, and myself. No one else knew of the study during the period between February 27, 1950, when the first child was fed the virus and late January, 1951, when observation of the first series of 20 subjects was nearing completion and preliminary evaluation of the procedure indicated that it was harmless.

The Ceryneian Hind

To compare the attenuation of a virus with Heracles' task of taming the Ceryneian Hind is to indulge in what might seem to be exaggeration, but the two tasks are both arduous and time-consuming. Attenuation of poliovirus can most easily be defined as loss of pathogenicity for man, but retention of all antigenic qualities for immunization purposes. Our understanding of the phenomenon of attenuation is very scanty because it has to be judged in relation to virulence, and virulence is one of the scientific terms most easily escaping correct interpretation, particularly in the field of polio research. When the work on polio began in our laboratories in 1947, the criterion for virulence of a poliovirus was its ability to cause paralysis upon direct inoculation into the nervous system of a primate. This criterion is still used to-day, and yet it is, and will, remain a highly artificial one until we can explain the factors determining the presence or absence of paralysis in cases of polio infection in man.

It should be remembered that there is no direct evidence that polio strains isolated from human paralytic cases are all virulent for the central nervous system of monkeys. Conversely, there is evidence for a marked variation in pathogenic properties for monkeys of virus strains isolated from polio-infected but asymptomatic children (Sabin, 1957), but this does not contribute much toward clarification of the problem. Furthermore, the term "virulence" or "neurovirulence" is often misinterpreted as referring to the character of the virus only, with complete disregard of the host. Yet such factors as age (Horstmann, 1955), peripheral trauma, exercise, and stress (Horstmann, 1950) play an important part in the determination of the virulence of a given strain. It has even been proposed that the host factors may be more decisive in the final outcome of a polio infection than the character of the virus (Shope, 1957).

To return from this digression on the theme of attenuation and virulence to the early history of the development of poliomyelitis vaccine, studies on the TN strain of type II virus were conducted for two to three years prior to feeding the virus to man (Koprowski *et al.*, 1951). Since tissue-culture techniques were not available at that time, the virus was subjected, as mentioned before, to numerous passages in laboratory rodents such as cotton-rats and mice and tested sporadically in monkeys for intracerebral pathogenicity.

The same procedure was used for the attenuation of type I virus, which, in contrast to type II, is responsible for most cases of paralytic poliomyelitis throughout the world. In 1952 a mixture of two type I strains, one the virulent Mahoney virus and the other a relatively mild strain called Sickle virus, was injected into mice, using a technique of intraspinal inoculation newly developed by Li and Schaeffer (1953). After adaptation of either the Sickle or the Mahoney virus, or both, to growth in the central nervous system of the mouse, this strain was serially transferred through 27 passages in mice. In 1953 it was judged sufficiently non-pathogenic for monkeys (Koprowski *et al.*, 1954) to be considered as a "candidate" for oral administration to children. By then, thanks to the work of Enders, Weller, and Robbins (1949), tissue-culture systems became available for the study of virus infections, including polio. This method was used in preparing the SM strain of type I virus for administration to man and for the laboratory tests on material excreted by children who were fed the virus.

In 1953 and early in 1954 Jervis, Norton, and I fed the attenuated type I virus to three children who had no antibodies against type I virus (Koprowski *et al.*, 1954a). Again, this was the first attempt to immunize a child against the dreaded paralysis-inducing type I virus by oral administration of an attenuated strain. Two children received type I virus alone, and one, who was also non-immune to type II virus, received a mixture of two attenuated viruses: TN (type II) and SM (type I). None of the children showed any signs of illness and all developed antibodies against the virus they were fed. The child who received a mixture of the two strains developed antibodies against both viruses. Thus a new principle was established, indicating the possibility of immunization by oral feeding of a combination of two or more strains of polio administered simultaneously (Koprowski *et al.*, 1954a). Investigation of the pathogenicity of the attenuated type I virus after passage through the human intestinal tract was included in this study, and showed that passage through man did not result in exacerbation of pathogenicity as tested in monkeys. This completed the first phase of the study of attenuation in the laboratory of two strains of poliovirus which were used successfully for oral immunization of man. The laboratory part of this study was done at Lederle Laboratories.

Other Methods, Other Workers

I will now summarize work by other investigators, employing sometimes similar and sometimes different methods. Roca-Garcia and his colleagues (1952), who were also working at Lederle Laboratories, introduced the use of the chick embryo as another host for adaptation and possible attenuation of poliovirus. They succeeded in infecting a developing chick embryo with a hamster-adapted (Moyer *et al.*, 1952) strain of type II virus (the MEF_1 strain). After 71 passages in chick embryo this egg-adapted strain showed low paralytogenic properties when injected intracerebrally into monkeys (Roca-Garcia and Jervis, 1955). Several years later (in 1956) it was tested for its immunizing capacity in man; however, its ability to establish intestinal infection was found to be poor and its immunizing properties were not outstanding (Roca-Garcia *et al.*, 1956). Progeny of this strain, isolated from virus plaques on monkey-kidney-tissue-culture system, failed in the hands of Plotkin, Koprowski, and Stokes (1959) to establish alimentary infection and antibody response in three out of four infants fed the virus.

In 1954 Li and Schaeffer published their studies on adaptation of the Mahoney type I strain to laboratory mice. The resulting variant was then passaged through monkey-testis culture and monkey skin (Li *et al.*, 1955), yielding a virus of low paralytogenicity for primates. This was made available to Sabin, under the name of LSc strain, and after further studies of attenuation is used to-day by Sabin as a type I vaccine. In 1954 Sabin *et al.* published their first study dealing with laboratory investigations of variants of poliovirus. In the attempt to attenuate the virus Sabin (1955a) made several passages of polio strains every 24 hours in tissue culture, using massive doses of virus as inoculum. At the end of such a passage cycle one passage was made with a very dilute virus inoculum in order to "catch" particles with low pathogenic properties. In 1955 Sabin published a study of feeding of a small number of human subjects with attenuated strains which were subsequently discarded (Sabin, 1955b).

The Stables of Augeias

The introduction by Dulbecco and Vogt (1954) of tissue-culture techniques, which made possible selection of the progeny of isolated particles of a virus and the application of this technique to polio research, has greatly facilitated investigations on the development of attenuated strains. The stables of viruses created by the methods described above—methods which in the light of the new knowledge were rapidly becoming obsolete—could now be cleansed. Though Heracles was to clean the cattle yards of Augeias in one day, "cleaning" of the stables of attenuated viruses was a more time-consuming, though certainly less arduous, task. Instead of diverting the rivers Alpheus and Peneius to flush out the yards, the "cleansing" was done by plating out viruses on tissue-culture monolayers, discarding specimens more pathogenic for monkeys, and subjecting those less pathogenic to repeated "purification," using the same process over and over again.

Variants of all strains of live virus used to-day for oral immunization of man have been selected by this method. The term "selection" instead of mutation is used purposely. There is no available evidence indicating that the long and arduous process of attenuation as applied up to now is anything else than cleaning of a stable of "white-legged black bulls, red stud bulls, and ferocious silvery-white bulls," paraphrasing again from the labours of Heracles. The more ferocious beasts are left behind, the tame animals are selected for breeding, their progeny again are screened for mild character, bred again, and so continued. Those who know their mythology will remember that in spite of solemn promises Heracles received no award for his labour. Augeias even denied that he and Heracles had struck a bargain. Familiarity with the story of live virus vaccine against polio makes one sometimes wonder if one is dealing with a *historical* myth only.

Como tu mi vuoi

More extensive laboratory studies during the past three years permitted characterization of the attenuated strains of polioviruses according to markers other than pathogenicity for monkeys. The death or survival of a monkey injected intraneurally with poliovirus is not an exact criterion of attenuation for man, and the use of many monkeys is expensive. These "laboratory" markers have been developed by several groups of investigators and relate to the following properties of an attenuated strain as compared with a virulent virus: poor growth in tissue cultures kept acid under low bicarbonate content (Dulbecco, 1954); poor growth in tissue cultures of a stable line of monkey-kidney cells in contrast to excellent growth in fresh explants of monkey kidney (Kanda and Melnick, 1959); and high sensitivity to development under high temperatures (Lwoff and Lwoff, 1959).

Estimation of these characters is not a simple laboratory procedure, since knowledge of the existence of the markers is based on the study of kinetic reactions following observation of growth of viruses in one or another system under different conditions. However, these characters of virus have enabled us to "mark" the attenuated viruses. Another extremely useful tool has been developed recently in connexion with serological differentiation of strains of polio within the same type. Studies of Wenner *et al.* (1956), McBride (1959), Gard (1960) and Wecker (1960) indicate that a given strain of a given type can be "marked" serologically so that it can probably be "spotted" at any given moment in its peregrinations. The existence of these markers may finally lead to achievement of the most important goal in the laboratory study of poliovirus: true mutation through chemical change of the infectious nucleic acid. In contrast to selection, which is a somewhat haphazard and prolonged process of attenuation, mutation may in one or two steps radically change the character of the virus.

"On ne badine pas avec l'hôte'"

The study of the virus as a virus and not as an entity eliciting response from its animal host is an art, but an abstract art. Piet Mondrian and Jackson Pollack are great painters, but in their special genre. Introduction of the virus into a living host and the reaction of the latter find no parallel in the test-tube. In the case of poliovirus the only real host is the human subject, since he represents the only true susceptible species and has no counterpart in the animal kingdom. In 1953 Jervis, Norton, and I "communicated" to the National Academy of Sciences (Koprowski *et al.*, 1954) results of a comparative study on oral administration of poliomyelitis virus to man and ape. The results are shown in the accompanying Table which is reproduced

*Results of Oral Administration of TN Strain to Three Species of Primates**

Pool No.	Species	Dose of Virus (ml.)	Total No. Fed	No. Excreting Virus	No. Showing Antibodies	Range of Antibody Titre
16	Man ..	1, 5, or 10	9	7	9	1:20–1:500
	Chimpanzee	10	2	1	2	1:85–1:95
21	Man	10	2	1	2	1:60–1:700
23	Man	10	5	3	5	1:32–1:2,500
24	Man	5 or 10	8	5	8	1:10–1:600
F_1	Chimpanzee	2×10	3	1	3	1:7 –1:300
31	Man ..	5	54	31	54	1:15–1:500
31	Chimpanzee	10	4	0	4	1:2 –1:35
31	Cynomolgus	3×2	11	0	0	—
31	Cynomolgus	2×6	5	0	0	—
YHP N–63	Cynomolgus	3×2	5	1	2	1:2
Grand total	Man ..	—	78	47	78	—
Grand total	Chimpanzee	—	9	2	9	—
Grand total	Cynomolgus	—	21	1	2	—

* In no instances included in this table were signs of illness noted. (Table reproduced from *Proceedings of the National Academy of Sciences*, **40**, 36, 1954.)

from that paper. Here an attenuated type II TN strain was fed to man, chimpanzees, and cynomolgus monkeys. The response in monkeys was poor, in chimpanzees intermediate, and in man excellent. We ended the paper by saying: "It is also clear that for certain questions the crucial answers may have to be sought in man himself, since data obtained in animals may be inadequate."

The Apples of Hesperides

In 1951 the first phase of the original field trial was completed. Confirmation of the results of the trial and more extensive study of reactions in the human host was the next step, and for this it became urgent to arrange for expansion of research in human subjects. The eleventh labour of Heracles was to be undertaken. A fateful meeting took place in New York in the Barbizon Plaza Hotel on January 19, 1952, between Dr. Smadel, at present Associate Director of the National Institutes of Health, Dr. K. F. Meyer, Director of the Hooper Foundation at the University of California, and myself. I was looking for counsel from Nereus and Prometheus. Dr. Smadel was familiar with our work on the immunization of man with living poliovirus and suggested to Dr. Meyer and myself that we establish a co-operative study. This led to prolonged and fruitful collaboration, when the search for the golden apples of the Hesperides was conducted near the Golden Gate, more precisely, in Jack London's *Valley of the Moon*. Dr. T. L. Nelson, Superintendent of the Sonoma State Hospital, became an active collaborator in the study, which began in 1952 and had as its aim elucidation of the following points in the virus–human host interaction:

1. The smallest dose of the attenuated virus which will still infect the human intestinal tract.
2. The duration of intestinal infection and the extent of spread of the virus from the virus-fed subject to non-vaccinated, non-immune contacts.
3. Existence of interference between two or more strains administered simultaneously.
4. Problems concerning different vehicles for feeding the virus.
5. Serial passages of the attenuated strains in human subjects.
6. Administration of attenuated virus in the presence of passively acquired antibody.
7. Local resistance of the human intestinal tract elicited by exposure to attenuated virus.

Plucking of the golden apples in this eleventh labour of Heracles took several years, but the results (Koprowski *et al.*, 1956) of the investigations were very gratifying. The minimum infective dose of type I virus, the then used SM strain, for the human intestinal tract was the equivalent of 2–20 plaque-forming units of the virus. It should be mentioned in passing that infectivity for the intestinal tract of strains of live poliovirus at present available varies considerably (Koprowski, 1958), and that this property may determine the degree of spread of a given virus: those which infect in a smaller dose spread more easily. The duration of intestinal infection varied from 16 days to 104 days for type I virus. (In another study (Koprowski *et al.*, 1956) the record length was extended to 171 days.) The spread of virus occurred from six children who were fed virus to 5 out of 15 type I non-immune contacts, but not to seven non-immune nurses. Administration of more than one strain simultaneously led occasionally to interference—that is, suppression of infection and of antibody induction by one of the strains (Koprowski, 1955).

Administration of one virus to a subject already excreting the other virus which had been fed some time before was an easy method of overcoming interference. Sabin has also observed interference between three polio types administered simultaneously, and suggested feeding the three types in a certain sequence (Sabin, 1956). In the hands of Plotkin, Koprowski, and Stokes (1959), however, this actual sequence of administration of poliovirus types played no part. The only important factor was the spaced feeding. More recent data (Benyesh-Melnick *et al.*, 1959; Horstmann *et al.*, 1959) obtained from the field indicate that the presence of other enteroviruses may interfere with the seeding of the intestinal tract by attenuated poliovirus, and that in some parts of the world, particularly tropical and subtropical areas, such interference may be a difficult problem to overcome. Conversely, opinions have been expressed, particularly by the Russian scientists (M. P. Chumakov, personal communication), to the effect that re-exposure to the attenuated virus, spreading from members of a "non-vaccinated" community, may vaccinate an individual who failed to become immunized on the first attempt either because he had been fed three polioviruses simultaneously or because an enterovirus was present in his intestinal tract.

Results of studies conducted in California have also indicated that the virus can be administered to human subjects in different forms, and that when it is fed in a capsule it will produce intestinal infection but cannot be recovered from the region of the pharynx. These results were confirmed by a study of Paul *et al.* (1957).

Attempts to limit the period of intestinal infection have failed. We are not familiar with any drug that could prevent further spread of the virus, nor is there any known agent for such limitation other than the properties inherent in the virus itself.

One of the last phases of the study in California was conducted in co-operation with Dr. T. L. Nelson, and consisted of serial passages of type I attenuated strain of poliomyelitis virus in man (Nelson and Koprowski, 1957). In this study a type I non-immune child was fed the vaccine and the virus was isolated from the faecal material. The resulting suspension was tested in monkeys, first by the intracerebral and later, in the trials, by the intraspinal route. If no exacerbation of neurovirulence for monkeys was observed—and this was the case—it was made into a bacterially sterile suspension and administered orally to another type I non-immune child, and so on. The results of intracerebral inoculation of the faecal virus preparation into cynomolgus monkeys failed to show an increased pathogenicity in the course of six serial passages of the virus in man. This was confirmed several years later by Smorodintsev (1959) in Leningrad. It should be noted that the type I virus which we are at present employing in mass vaccination programmes does not originate from that used in the initial vaccinations in 1953–6, but was isolated from a child fed the fourth human passage of the virus (Nelson and Koprowski, 1957). This strain was again subjected to numerous laboratory procedures at the Wistar Institute for selection of the least virulent particles, and represents a different strain from that used originally.

Administration of gamma-globulin to children at the time of virus-feeding had no effect whatsoever on the incidence and duration of intestinal infection or active antibody response (Koprowski *et al.*, 1956). In the California study we have observed for the first time local resistance of the intestinal tract of children to reinfection with the TN type II virus three years after the first feeding (Koprowski *et al.*, 1956). These results have been extended to work done with the type I virus (Koprowski, 1958). Subsequently, Fox *et al.* (1957) and Horstmann *et al.* (1957) have shown the same intestinal resistance to infection upon exposure to an attenuated strain in subjects with naturally acquired antibodies. Sabin (1957) has also observed local intestinal resistance to reinfection with the same strain in a certain proportion of subjects when he fed the attenuated strains.

"The Child is Father to the Man"

"Is he? Then in the name of common sense why do we always treat children on the assumption that the man is father to the child?" (G. B. Shaw, *Prefaces.* Constable, London, 1939).

One of the most important aspects of the study of virus–host relationship is the susceptibility of the host at different ages to a virus infection. In order to elucidate these factors in the field of live attenuated poliovirus, a collaboration was established with Dr. Joseph Stokes, of Philadelphia, during the early phase of the original investigations. Studies conducted in co-operation with Dr. Stokes, and later with my colleagues, Drs. Plotkin and Pagano, concentrated on the problem of vaccination of infants less than 6 months old. Preliminary results indicated that infants less than 6 months old can be successfully immunized against poliomyelitis through feeding (in formula) of living attenuated virus (Koprowski *et al.*, 1956), even in the presence of transplacentally acquired passive antibodies.

Similar studies later conducted elsewhere (Martins Da Silva *et al.*, 1957) indicated the complete harmlessness of such an immunization procedure. Infants 2 months of age or older developed intestinal infection at the same rate as older children or adults, and those less than 2 months old were slightly more resistant to the same dose of virus (Plotkin, Koprowski, and Stokes, 1959). However, when the dose of attenuated virus was increased tenfold or hundredfold over that usually fed to older children, establishment of intestinal carrier state, followed by the development of antibody, took place even in infants who ingested virus within a few hours after birth (Plotkin, Koprowski, and Stokes, 1959). Infants who fail to be immunized after the first feeding of virus can be successfully immunized by the same dose repeated when they are somewhat older, thus excluding the possibility that administration of an infectious agent immediately after birth may lead to tolerance and inability to develop protective antibodies later in life. Following administration of virus the passively acquired transplacental antibodies "blend" into the active antibody, which was found to persist after a single feeding of virus for a period exceeding three years (the longest so far tested) (Plotkin *et al.*, 1959).

There is great attraction in the thought that perhaps the newborn population is the ideal population to receive live virus and that too little emphasis has been placed on the host, who in the end reacts to the virus infection. In summary, it may be pointed out that there are numerous advantages in the immunization of young infants against poliomyelitis with living attenuated virus vaccine:

1. The virus can be administered within hours after birth when the newborn are in the hospital, or, if at home, are still under the immediate care of a physician or a midwife. This may assure a more proper administration of the vaccine.

2. Administration of the virus at a time when relatively high levels of transplacental antibodies are present in the serum of the recipient allows "blending" of these antibodies into the virus-induced active type of antibody.

3. Either because of shorter duration of intestinal infection, or because of factors not as yet clearly known, the spread of virus from the vaccinated infant less than 6 months old to his surroundings does not occur very often.

4. In countries where visits to paediatricians or clinics at definite intervals after birth are routine, administration of the two other types of virus may coincide with such visits, thus assuring a proper vaccination procedure. It should be emphasized that in view of the preponderant role of type I virus as the cause of paralytic poliomyelitis, it is our opinion that attenuated type I virus should be administered first. In this way, protection against the greatest menace is guaranteed, even if for some reason the child is never fed the other two types of virus.

5. Immunity after feeding virus to a newborn infant is long-lasting. It is possible that it may last for years, perhaps even a lifetime. There are, of course, no objections to refeeding the virus at certain intervals during the life of an individual who was vaccinated as a newborn. However, so far there are no indications that this is necessary.

6. Last, lack of opportunity for enteroviruses other than poliovirus to infect the intestinal tract of a newborn within hours after birth eliminates interference and assures successful outcome of the vaccination procedure.

"From Here to Eternity"

Immunity after the administration of living virus may well last "from here to eternity" or "from cradle to grave." Children fed the old TN virus in 1950 (Koprowski *et al.*, 1952) have antibodies against type II virus eight to nine years later, the longest period so far tested (Plotkin *et al.*, 1959). Type I poliomyelitis antibody was present in seven children who were fed the SM strain four years ago, including one who was fed the mixture of type I and II and is still immune to both types. As mentioned before, virus-fed infants retained immunity for a period of two years, and will probably be immune long thereafter. Because of the "head start" of our group in this study, others have not as yet had an opportunity to investigate duration of immunity in subjects they had immunized. However, in a recent communication Sabin (1959) describes persistence of homotypic antibody in five children and six adults fed all three types two years previously. When re-exposed to a massive dose of virus, marked local intestinal resistance was observed against types I and II virus, but the evidence of reinfection with type III virus was frequent.

Tactical Exercises

Thus we have travelled a long way since the time when the attenuated virus was first used. Then, when the work began, it was difficult to project into the future a present that contained only 20 subjects successfully immunized through feeding of the virus. New faith had to be created, since the existing faith was in the development of inactivated virus vaccine only. It was also not too easy to bring over to our side the indifferent and the undecided, since my associates and I were alone in this field when the work began, and remained so for

several years. Gradually, however, other scientists became aware of this problem and joined us in this field of endeavour, which by then was developing rapidly.

In 1957, at the end of what may be called the first era of the history of live virus vaccine, all available experimental and clinical evidence pointed to the conclusion that live attenuated viruses seemed to be safe for use in man. An attempt to organize a field trial of larger magnitude was clearly indicated, and an opportunity for a real "break-through" came when co-operation was established between the Government of the Belgian Congo and ourselves. During 1957 the number of inhabitants of the Belgian Congo who had been fed live virus was rising rapidly, and the "climax" occurred in the beginning of 1958, when a mass vaccination trial of 215,000 subjects, fed the virus at a rate of 12,000 people a day, was organized by Courtois, Jervis, Flack, and myself in the Ruzizi Valley (Courtois *et al.*, 1958). I have found the shortest and best description of this first large-scale live-polio trial in an article published by Chumakov (1959) in connexion with the polio trials conducted in Russia. He said—and I am quoting, translating from Russian—"We have adopted (for the purpose of the Russian trials) a procedure chosen by Dr. Koprowski, who successfully employed the attenuated type I poliovirus (substrain CHAT of strain SM) in the Belgian Congo in 1958 for oral immunization of more than 320,000 children against poliomyelitis. No complications or cases of poliomyelitis were observed among the vaccinated or among subjects who were in contact with the vaccinated individuals."

The Belgian Congo trials have enlarged considerably, and during 1959 75,000 children aged 0–5 years have been vaccinated in Leopoldville (Plotkin *et al.*, 1960). More vaccination campaigns organized in several provinces of the Belgian Congo are raising the number of vaccinated individuals into millions. After preliminary field investigations (Przesmycki *et al.*, 1959) 10 million children and adolescents in Poland are being vaccinated now. Buser and Schär (1958), in Switzerland, and Gard *et al.* (1959), in Sweden, are carefully enlarging their preliminary trials. Russian scientists (Chumakov *et al.*, 1959) in an energetic campaign have immunized millions of subjects with live virus vaccines. Immunization campaigns have been started in South America and Mexico (various authors, 1959). Thus, from a rather modest beginning the live virus vaccination mushroomed during the last two years into a project of considerable size.

Envoi

The history I have just given of the development of live virus vaccine is my attempt to "tell you the origin of wheat." I should not be surprised, however, if you at some time or other hear a different version, put forth by those scientists who follow Schopenhauer's advice on merit: "There are two ways of behaving in regard to merit: either to have some of one's own, or to refuse any to others."

Now that I have talked at such length in my effort to substitute facts for some of the myths surrounding the origin of attenuated poliovirus vaccine, I realize that the time has come to end this talk on justification of my performance.

In the words of Pascal (1656): "Je n'ai fait celle-ci plus longue que parce que je n'ai pas eu le loisir de la faire plus courte."

References

Benyesh-Melnick, M., Melnick, J. L., and Ramos-Alvarez, M. (1959). "Poliomyelitis Infection Rate Among Mexican Children Fed Attenuated Poliovirus Vaccines." Presented at the 1st International Conference on Live Poliovirus Vaccines, Pan American Health Organization and World Health Organization, Washington, D.C., June 22–6, 1959.

Buser, F., and Schär, M. (1958). *Schweiz. med. Wschr.* **88**, 1282.

Chumakov, M. P. (1959). "Methodicheskie Ukasania po Organesacii i Provedeniu Profilaktecheskich Peroralnich Provivok Shivoj Attenuirovannoj Vakccinoj Protiv Poliomielita." Academia Medicinskich Nauk S.S.S.R., Institut po Isuscheniu Poliomielita, Moscow.

—— Voroshilova, M. K., Vasilyeva, K. A., Bakina, M., Dobrova, I. N., Drosdov, S. G., Podsedlovsky, T. S., Kostina, K. A., Shirman, G. A., Yankevich, O. D., and Uspensky, U. S. (1959). Preliminary report on mass oral immunization of population against poliomyelitis with live virus vaccine from A. B. Sabin's attenuated strains. Institute for Poliomyelitis Research, Academy of Medical Sciences, U.S.S.R., Moscow.

Courtois, G., Flack, A., Jervis, G. A., Koprowski, H., and Ninane, G. (1958). *Brit. med. J.*, **2**, 187.

Dulbecco, R. (1957). In *Cellular Biology, Nucleic Acids and Viruses*, by V. G. Allfrey *et al.* Special Pub. New York Acad. Sci., No. 5, p. 138.

—— and Vogt, M. (1954). *J. exp. Med.*, **99**, 167.

Enders, J. F., Weller, T. H., and Robbins, F. C. (1949). *Science*, **109**, 85.

Fox, J. P., Gelfand, H. M., LeBlanc, D. R., and Conwell, D. P. (1957). *Amer. J. Hyg.* **65**, 344.

Gard, S. (1960). *Bull. Wld Hlth Org.*, **22**, 235.

—— Böttiger, M., and Lagercrantz, R. (1959). "Vaccination with Attenuated Poliovirus, Type I, the CHAT Strain." Presented at the Conference on Live Poliovirus Vaccines, Pan American Health Organization and World Health Organization, Washington, D.C., June 22–6, 1959.

Horstmann, D. M. (1950). *J. Amer. med. Ass.*, **142**, 236.

—— (1955). *Ann. N.Y. Acad. Sci.*, **61**, 956.

—— Niederman, J. C., Melnick, J. L., and Paul, J. R. (1957). *Trans. Ass. Amer. Phycns*, **70**, 91.

—— —— and Paul, J. R. (1959). *J. Amer. med. Ass.*, **170**, 1.

Kanda, Y., and Melnick, J. L. (1959). *J. exp. Med.*, **109**, 9.

Koprowski, H. (1955). *Ann. N.Y. Acad. Sci.*, **61**, 1039.

—— (1958). Poliomyelitis: Papers and Discussions presented at the Fourth International Poliomyelitis Conference, Geneva, 1957, p. 112.

—— Jervis, G. A., and Norton, T. W. (1952). *Amer. J. Hyg.*, **55**, 108.

—— —— —— and Norton, T. W. (1954a). *Proc. Soc. exp. Biol. (N.Y.)*, **86**, 244.

—— —— —— (1954b). *Proc. nat. Acad. Sci. (Wash.)*, **40**, 36.

—— —— —— and Pfeister, K. (1954). *Proc. soc. exp. Biol. (N.Y.)*, **86**, 238.

—— Norton, T. W., Hummeler, K., Stokes, J., jun., Hunt, A. D., jun., Flack, A., and Jervis, G. A. (1956). *J. Amer. med. Ass.*, **162**, 1281.

—— —— and Jervis, G. A. (1951). *Bact. Proc.*, p. 92 (abstract).

—— —— —— Nelson, T. L., Chadwick, D. L., Nelsen, D. J., and Meyer, K. F. (1956). *J. Amer. med. Ass.*, **160**, 954.

—— —— —— Stokes, J., jun., McGee, E. L., and Nelsen, D. J. (1956). *Amer. J. med. Sci.*, **232**, 378.

Li, C. P., and Schaeffer, M. (1953). *Proc. Soc. exp. Biol. (N.Y.)*, **82**, 477.

—— —— (1954). Ibid., **87**, 148.

—— —— and Nelson, D. B. (1955). *Ann. N.Y. Acad. Sci.*, **61**, 902.

Lwoff, A., and Lwoff, M. (1959). *Compt. r. Acad. Sci. (Paris)*, **243**, 154.

McBride, W. D. (1959). *Virology*, **7**, 45.

Martins Da Silva, M., McKelroy, J., Baume, H., Prem, K. Cooney, M., and Johnson, E. (1957). *Univ. Minn. med. Bull.*, **29**, 133.

Moyer, A. W., Accorti, C., and Cox, H. R. (1952). *Proc. Soc. exp. Biol. (N.Y.)*, **81**, 513.

Nelson, T. L., and Koprowski, H. (1957). Presented at the meeting of the Western Society for Pediatric Research, San Francisco, October 28–9, 1957. Summarized in Special Pub. New York Acad. Sci., No. 5, p. 128.

Pascal, B. (1656). *Lettres écrites à un Provincial.* Paris, 16th letter.

Paul, J. R., Horstmann, D. M., Melnick, J. L., Niederman, J. C., and Deutsch, J. (1957). "Immunization Against Poliomyelitis: Killed Vaccine Followed by Induced Infection with Live Virus." In *Cellular Biology, Nucleic Acids and Viruses*, by V. G. Allfrey *et al.* Special Pub. New York Acad. Sci., No. 5, p. 141.

Plotkin, S. A., Jervis, G., Norton, T., Stokes, J., jun., and Koprowski, H. (1959). *J. Amer. med. Ass.*, **170**, 8.

—— Koprowski, H., and Stokes, J., jun. (1959). *Pediatrics*, **23**, 1041.

—— Lebrun, A., and Koprowski, H. (1960). *Bull. Wld Hlth Org.*, **22**, 215.

Przesmycki, F., Dobrowolska, H., Olakowski, T., Stańczyk, R., and Naruszewicz, D. (1959). Report on field trials with live attenuated poliomyelitis vaccine in Poland. Presented at the Conference on Live Poliovirus Vaccines, Pan American Health Organization and World Health Organization, Washington, D.C., June 22–6, 1959.
Roca-Garcia, M., and Jervis, G. A. (1955). *Ann. N.Y. Acad. Sci.*, **61**, 911.
—— Koprowski, H., Jervis, G. A., Norton, T. W., Nelson, T. L., and Cox, H. R. (1956). *J. Immunol.*, **77**, 123.
—— Moyer, A. W., and Cox, H. R. (1952). *Proc. Soc. exp. Biol. (N.Y.)*, **81**, 519.
Sabin, A. B. (1955a). *Ann. N.Y. Acad. Sci.*, **61**, 924.
—— (1955b). *Amer. J. med. Sci.*, **230**, 1.
—— (1956). *J. Amer. med. Ass.*, **162**, 1589.
—— (1957). Ibid., **164**, 1216.
—— (1959). "Recent Studies and Field Tests with a Live Attenuated Poliovirus Vaccine." Presented at the Conference on Live Poliovirus Vaccine, Pan American Health Organization and World Health Organization, Washington, D.C., June 22–6, 1959.
—— Hennessen, W. A., and Winsser, J. (1954). *J. exp. Med.* **99**, 551.
Saint-Simon at Versailles (1958). Selected and translated from the Memoirs of M. Le Duc de Saint-Simon by Lucy Norton. Harper Bros., New York.
Shope, R. E. (1957). In *Cellular Biology, Nucleic Acids and Viruses*, by V. G. Allfrey *et al.* Special Pub. New York Acad. Sci., No. 5, p. 139.
Smorodintsev, A. A. (1959). "Properties and Behaviour of Orally Administered Strains." Presented at the Conference on Live Poliovirus Vaccines, Pan American Health Organization and World Health Organization, Washington, D.C., June 22–6, 1959.
Various authors (1959). Papers presented at the Conference on Live Poliovirus Vaccines, Pan American Health Organization and the World Health Organization, Washington, D.C., June 22–6, 1959.
Wecker, E. (1960). *Virology*, **10**, 376.
Wenner, H. A., Kamitsuka, P., and Lenahan, M. (1956). *J. Immunol.*, **77**, 220.

EXCESSIVE PERINATAL MORTALITY IN A SMALL TOWN ASSOCIATED WITH EVIDENCE OF TOXOPLASMOSIS

BY

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During the years 1956, 1957, and 1958, large and persistent differences were noted between the perinatal mortality rates for three adjacent districts in North Lincolnshire. It was found that these differences were due to variation in the stillbirth rates. The small town of Barton-on-Humber suffered a stillbirth rate of 59.6 for the triennium (see Chart). During the same period the neighbouring town of Brigg enjoyed the exceptionally favourable stillbirth rate of 9.0, while the surrounding rural district experienced a rate of 28.1. It was found that the differences in numbers of stillbirths occurring in these districts (Tables I and II) were statistically significant ($\chi^2 = 14.98$; $P<0.001$). This paper describes the investigations which were made in an endeavour to ascertain the cause of the excess of stillbirths experienced in Barton-on-Humber.

TABLE I.—*Vital Statistics for Area*

	Barton-on-Humber U.D. (Pop. 6,420)			Brigg U.D. (Pop. 4,200)			Glanford Brigg R.D. (Pop. 33,200)		
	L.B.	S.B.	N.D.	L.B.	S.B.	N.D.	L.B.	S.B.	N.D.
1956 ..	101	8	3	68	1	2	493	18	7
1957 ..	104	5	3	65	1	2	535	19	6
1958 ..	95	6	0	68	0	2	563	9	9
	300	19	6	221	2	6	1,591	46	22

L.B. = Live births. S.B. = Stillbirths. N.D. = Neonatal deaths (i.e., deaths of infants during first four weeks of life).

TABLE II.—*Perinatal Mortality and Stillbirth Rates* (1956–8)

	Perinatal Mortality Rate*	Stillbirth Rate
Barton-on-Humber U.D. ..	78·4	59·6
Glanford Brigg R.D.	41·6	28·1
Brigg U.D.	35·9	9·0
England and Wales (1956) ..	39·2	22·9

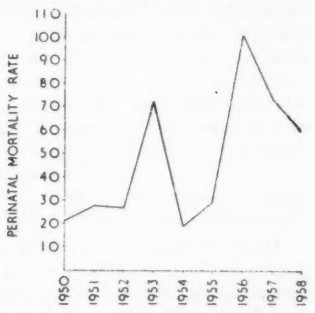
* Note the perinatal mortality rate used in this table is based on stillbirths and deaths below the age of 4 weeks. It differs from the perinatal mortality rate used by the Registrar-General, which only takes account of deaths in the first week of life in addition to stillbirths.

TABLE III.—*Incidence of Gross Malformation and Maceration, Glanford Brigg R.D.* November, 1958–December, 1959 (Preliminary Survey). See also Table VIII.*

	Grossly Malformed	Not Grossly Malformed	Total
Macerated ..	1	5	6
Not macerated ..	5	6	11
Total ..	6	11	17

* Rural district figures included, as only one stillbirth occurred in Barton-on-Humber in 1959.

By the end of 1957 it was already apparent that the excessive mortality in Barton was unlikely to be due to chance, and a preliminary survey was begun. The county medical officer of health kindly arranged for the midwives to complete a questionary in respect of all stillbirths and early neonatal deaths occurring in the three county districts. From these questionaries it soon became apparent that the foetus was either malformed or macerated in almost two-thirds of all stillbirths in the area (Table III). This suggested that the factors responsible must be non-obstetric, and any inquiry must take account of possible genetic and environmental influences if it was to be successful.



Perinatal mortality in Barton-on-Humber, 1950–8.

Environmental Factors

Environmental factors could be chemical, physical, or biological, and the ways in which the two towns might differ in respect of such factors were considered. Both are small market towns within 11 miles (17.7 km.) of each other. Barton is situated on the Humber bank, where the salt marshes and brackish water in old clay pits provide a breeding-ground for mosquitoes, whereas Brigg is situated 10 miles (16 km.) inland on the banks of the River Ancholme—a less favourable breeding ground. Brigg is situated on two main trunk roads and has good rail connexions, whereas Barton is not on any main route. There is a hospital at Brigg, while Barton is remote from hospital facilities. The only other obvious difference between the two towns is in the nature of the local industries. The principal industries in Brigg are fruit-canning, sugar-refining, and hosiery manufacture, while the major industries in Barton are the manufacture of bicycles, chemicals, ropes, and bricks.

Physical or toxic hazards resulting from the nature of local industries might play some part in causing differences in stillbirth rates, and could be investigated by ascertaining the nature of work done during early pregnancy. Remoteness from hospital facilities could

influence stillbirths in two ways. There might be a direct effect upon obstetric care, and there could be an indirect effect if this remoteness influenced the doctors' choice of treatment for other conditions. Drugs prescribed by doctors constitute an obvious possible source of toxic chemicals, and there is some evidence to suggest that drugs in use to-day may be harmful to the developing foetus. Allison McDonald's (1958) observation that there was a significant excess of severe congenital malformation in babies born to women with active or quiescent tuberculosis as compared with babies of mothers with arrested disease might reflect a toxic effect of anti-tuberculosis drugs. McCreary's (1959) assertion that overdosage of pregnant women with vitamin B_6 and with vitamin D leads to increased incidence of congenital abnormalities, and that the administration of cortisone to pregnant experimental animals caused a vast increase in the incidence of malformations, lends further support to this hypothesis. It was felt that inquiry into all drugs prescribed during gestation might indicate if such a factor was operative. Dental anaesthesia and treatment, and exposure to *x*-rays, were also included for investigation.

Genetic factors are more difficult to investigate ; but it was felt that, whether dominant, recessive, or multifactorial, they would result in a tendency for more than one foetus to be affected in the large families. An indication of this might therefore be gained from the obstetric histories. Stillbirths occurring in families of consanguineous parents would be suggestive of recessive inheritance. The fact that the stillbirth rate was higher in a town the size of Barton than in the surrounding small villages with their more inbred populations suggested that the cause was unlikely to be genetic.

The most hopeful line of inquiry was felt to be investigation of biological factors. Rubella and syphilis are known to be capable of harming a foetus, and Coffey and Jessop (1959) have demonstrated some correlation between history of influenza and the incidence of congenital malformation. No disease was known to be more prevalent in Barton-on-Humber than in Brigg at this time, and it seemed unlikely that any of the respiratory or E.C.H.O. virus infections could cause so localized an outbreak of such long duration. It seemed that the most probable biological agent would be an infection whose rate of spread was slow, and which was either symptomless or which produced vague or minor illness of a type seldom recognized. Brucellosis and toxoplasmosis were thought to fulfil these criteria.

Routine milk-testing had shown that cattle in the area were excreting *Brucella abortus* on a number of occasions during the years in question. Investigation of this disease was therefore deemed worth while. Toxoplasmosis had been shown by Beattie (1957) to be prevalent in Lincolnshire. His survey of blood donors in small towns and rural areas of Lincolnshire showed that in Brigg, where the stillbirth rate was 9.0, only 10% of blood donors had positive dye tests at a titre of 1/16, whereas 27% of blood donors from Brigg Rural District had positive dye tests. As the stillbirth rate for Brigg Rural District was 28.1 it appeared that stillbirths and toxoplasmosis might well be related.

On inquiry it was found that the dye-test survey had not included Barton-on-Humber, and that the specimens from Brigg rural area did not represent all parishes. Professor Beattie kindly proffered his help in investigating this problem. He offered to perform toxoplasma dye tests on blood from mothers of stillbirths, " control " mothers of live babies, and expectant mothers. He also agreed to carry out brucella agglutination tests on these blood specimens, and to do toxoplasma dye tests on blood from donors in the Barton area. Only the retrospective part of the investigation is included in this paper.

Method and Materials

The 19 women who were resident in Barton-on-Humber and had stillborn babies during 1956, 1957, and 1958 were identified and traced. For each of these women two " control " mothers of live babies born in the same month were selected. The method of selection was to ascertain whether the stillbirth had occurred in hospital or at home, and to take the two live births which were comparable in this respect and were nearest in time to the stillbirth. Only one control was used for each stillbirth. The " spare " one was used only where the first control had left the district or gave a history of previous stillbirth. The elimination from the control group of mothers who had suffered previous stillbirth was felt to be desirable, since such stillbirths might have been caused by the same factor as those under investigation. Only one was discarded on these grounds. Since none of the women whose stillbirths were to be investigated gave a history of previous stillbirth, it was thought that this would not result in bias.

A questionary was designed to obtain information regarding past obstetric history, consanguinity between parents, occupation of father, and details of work outside the home, illnesses during pregnancy, dental treatment, anaesthetics, *x* rays, medical treatment, recreational habits, and contact with animals, in addition to details of the pregnancy under review.

Each woman was interviewed by me, and the questionary was completed. A specimen of 10 ml. of blood was then taken and sent in a plain tube to Professor Beattie for dye testing and brucella agglutination. Questionaries were then sent to the general practitioners, who were asked to supply details of all drugs prescribed for these women during the period of gestation, and to give details of all diagnoses made. Details of the confinement were obtained from the midwife or doctor in attendance, or from hospital records. Records of blood-pressure readings and of urine tests during the antenatal period were obtained from both doctor and midwife independently.

Observations

The " control " and " stillbirth " groups were first compared in respect of age and parity. Concordance in these respects, though not perfect, was found to be tolerably good (Table IV).

Only two of the mothers of stillbirths undertook paid employment outside the home during the period of gestation, whereas five of the " control " mothers did so. The two who did work were a school teacher and an office worker, and both ceased work at the fourth month of pregnancy. It was possible, therefore, to eliminate industrial hazards as a cause of the high stillbirth rate.

No big discrepancies were noted between the two groups in relation to dental treatment, anaesthetics, exposure to *x* rays, minor illnesses, or illnesses for which the women consulted their doctors (Table V). It was found that in relationship to illnesses, however, the memories of the women proved unreliable. A number

TABLE IV.—*Maternal Age and Parity at Confinement*

	Age in Years			Parity								
	20–29	30–39	40–49	1	2	3	4	5	6	7	9	11
Stillbirths	11	7	1	4	6	4	1	2	1	—	1	—
Control ..	10	9	0	5	6	1	4	—	1	1	—	1

TABLE V

	Mother at Work Outside Home	Dental Treatment	Dental Anaesthetic: Gas	Dental Anaesthetic: Local	Exposure to X rays	No. of Mothers who had Minor Illness (Untreated)	No. of Mothers Claiming to have Received Treatment from Doctor	No. of Patients for whom Drugs were Prescribed by G.P.
Stillbirths ..	2	4	2	1	2	7	8	11
Control ..	5	5	3	1	1	5	7	10

who were unable to remember receiving medical treatment from their general practitioner were shown, on the record of drugs administered by the doctors, to have received treatment. In the case of some others who thought the doctor had treated them, there was no entry in the medical records at the doctor's surgery to support this. It is probable that the answers to the questions on minor illnesses, insect bites, etc., are equally unreliable.

From the doctors' records of drugs prescribed it was found that of the 17 mothers of stillbirths on whom information was available, drugs had been prescribed for 11, whereas of the 17 control mothers on whom such reports were obtainable, 10 had been treated. No single drug was prescribed for more than four patients in either group. The most frequently prescribed drug was phenobarbitone, which was taken by four women in each group.

Hypnotics, alkalis, and antipyretic analgesics were prescribed more often for the mothers of stillbirths than for the control mothers (Table VI). In each case the numbers involved are small and there is no indication that any drug was the cause of stillbirth. The biggest differences were: three mothers of stillbirths took magnesium trisilicate, compared with none of the controls; three mothers of stillbirths took amylobarbitone sodium, compared with none of the control mothers. It is felt that differences in drugs prescribed are more likely to reflect the symptomatology of the disease responsible than to be the cause of the stillbirths. The excess of hypnotics and analgesics suggests that a disease causing vague symptoms for which no cause could be found, and for which a neurotic cause may have been suspected, might have been responsible.

None of the women were blood relations of their husbands, and none of the mothers of the stillbirths gave a history of previous stillbirths. Three have a history of previous abortion, and among the control group there were two with such a history. One mother who had a stillborn baby had lost a former child seven months after birth as a result of hydrocephaly. Two of the mothers of stillbirths were sisters. Both the latter women had moderately high titres to the toxoplasma dye test, and both had titres of 1/160 to the brucella agglutination test.

TABLE VI

	Hypnotics: Phenobarbitone	Hypnotics: Amylobarbitone Sodium	Hypnotics: Pot. Brom.	Hypnotics: Chlorpromazine	Hypnotics: Total	Alkalis: Mag. Trisil.	Alkalis: Other	Alkalis: Total	Antipyretic/Analgesics: Aspirin	Antipyretic/Analgesics: A.P.C.	Antipyretic/Analgesics: Pannodol	Antipyretic/Analgesics: Total
Stillbirths ..	4	3	1	1	9	3	1	4	1	2	0	3
Control ..	4	0	0	0	4	0	1	1	0	0	1	1

The sister-in-law of these two women—wife of their brother—had produced a stillborn baby during 1955. It is therefore possible that a genetic factor might have been concerned in these instances, but the evidence is equivocal and no other evidence of a genetic cause was found.

Six of the stillbirths presented as breeches, compared with only two among the controls. One of the latter was treated by external version and delivered as a vertex. Two from the stillbirth group were "transverse lies." One was treated by internal version and delivered as a breech, the other was treated by caesarean section as labour was obstructed by a large fibromyoma which completely filled the pelvis. One of the stillbirths was the result of ante-partum haemorrhage due to marginal placenta praevia, and one of the controls was a persistent occipito-posterior which was treated by manual rotation and application of forceps. The remainder were normal deliveries.

Seven of the mothers of stillbirths had some degree of toxaemia of pregnancy, compared with four of the controls. Two of the toxaemic mothers gave birth to hydrocephalic stillborn infants.

TABLE VII.—*Incidence of Titres of Cytoplasm Modifying Toxoplasma Antibody*

Dye Test Result:	–	+1/4 −1/8	+1/8 −1/16	+1/16 −1/32	+1/32 −1/64	+1/64	Total
Stillbirths ..	0	1	3	2	7	6	19
Control	6	4	3	2	3	1	19

The serological findings are shown in Table VII. Regrettably, brucella agglutinations were not performed on some of the "control" bloods; but, since only two of the stillbirth group had positive tests, brucellosis can safely be eliminated as a major factor in causing the excess of stillbirths.

It can be seen from Table VII that the distribution of dye-test titres for toxoplasmosis varies greatly between the stillbirth and control groups. Most of the blood specimens from mothers of stillbirths were positive at titres above 1/32, whereas most of the "control" bloods were negative at 1/16. These differences are statistically significant. χ^2 (using Yates's correction) is 6.80 ($0.01 > P > 0.001$) when the test is done comparing the numbers giving positive and negative tests at titres of 1/16 and 1/32.

It will be seen that there is an excess of nine women with dye-test titres above 1/32 in the stillbirth group. Most of the toxoplasma-dye-test titres were very much lower than one expects to find shortly after an acute infection. As the tests were performed from one to four years after the pregnancies, during which infection was suspected, very high titres were not expected. In the stillbirth group the six highest were 1/600, 1/320, 1/110, 1/78, and two at 1/64. In the control group one woman had a titre of 1/8,000 and there were two with titres of 1/48, one of 1/32, and two of 1/18. The

woman whose titre was 1/8,000 had her blood taken for test on December 1, 1959. She had her last baby in March, 1957. Slight symptoms during the summer of 1959 may have been due to infection at this time.

Discussion

Since foetal mortality is higher in breech deliveries than in normal confinements, any series of stillbirths is likely to show a higher incidence of breech presentations than would be found in a control series. Only one of the stillborn breeches in this series was a domiciliary confinement; the rest were delivered in the same hospitals which serve the other two areas. The proportion of breeches is double that found in the series of stillbirths from the rural district on which reports were obtained. This suggests that during the years in question there was a real increase in incidence of breech presentations in women resident in Barton-on-Humber. Such an increase could be caused by any factor which altered the relative proportions of the foetal head and the available space in the maternal pelvis. Any condition which renders the foetal head larger or smaller than normal, or which causes a space-occupying lesion within the mother's pelvis, would tend to prevent "fixing" of the foetal head and predispose to malpresentation. Since congenital toxoplasmosis is stated by Feldman and Miller (1956) and Feldman (1958) to cause hydrocephaly in 22% of cases and microcephaly in a further 21%, a high incidence of malpresentation could well be caused by this condition. Three of the six breech stillbirths in this series were not due to obstetric factors, for one was both macerated and hydrocephalic, another was macerated, and the third was hydrocephalic. Such cases could well be caused by a disease such as toxoplasmosis.

In only 3 of the 19 stillbirths is it possible to state the cause with any certainty. In one case the foetal heart stopped after the mother was injured in a fall at the 27th week of pregnancy. Three weeks later she went into labour and was delivered of an immature macerated foetus. In another patient the transverse lie of the foetus was due to a large fibromyoma which filled the pelvis and to which a low-lying placenta was adherent. In this case labour was obstructed by the fibroid and caesarean section was necessary, though the baby was already dead. In a third case there was a placenta praevia and the cord encircled the baby's neck.

Though toxaemia was more frequent in the stillbirth group the difference in incidence was not significant ($\chi^2=0.50$; $0.5>p>0.3$). All the toxaemic mothers in both groups had positive dye tests.

The most notable difference between the two groups was in respect of toxoplasma-dye-test titres. Since this was the only difference between the groups that was statistically significant it is necessary to consider the hypothesis that some of the stillbirths might have been caused by this disease.

Though Nicolle and Manceaux (1908) described *Toxoplasma gondii* over 50 years ago, it was not until 1939 that Wolf, Cowen, and Paige proved by isolating the parasite that it caused congenital disease in man. Since then a great many cases have been described by these and other workers. Congenital toxoplasmosis may vary in severity between infections so severe as to result in stillbirth, and infections so mild that the baby appears normal at birth, but develops symptoms subsequently. Sabin (1942) described the syndrome of hydrocephaly or microcephaly, chorioretinitis, convulsions or other neurological signs, and cerebral calcifications, but any of these may occur alone, the commonest manifestation being chorioretinitis. Another manifestation of the disease is recorded by Bain *et al.* (1956), who describe three cases with features resembling haemolytic disease of the newborn. Two of these were stillborn, the third dying soon after birth.

TABLE VIII.—*Incidence of Hydrocephaly and Maceration (Barton-on-Humber, 1956-8)*

	Hydrocephaly	Not Hydrocephalic	Total
Macerated	2	8	10
Not macerated ..	2	7	9
Total ..	4	15	19

It thus appears that stillbirth may be caused by toxoplasmosis, either primarily as a result of the infection or secondarily as a result of obstetric difficulty due to hydrocephaly or malpresentation. Consequently the finding of a significant excess of toxoplasma-dye-test titres in mothers of stillbirths (Table VII) supported by a relatively high incidence of hydrocephaly (Table VIII) suggests that toxoplasmosis may have caused a proportion of these stillbirths.

Before this hypothesis can be accepted it is necessary to consider whether the dye-test titres observed are compatible with infection at the time of the pregnancy in question. This involves consideration of: (*a*) the date when maternal infection must have occurred; (*b*) the rate of rise and fall of dye-test titres after adult infection; and (*c*) the interval between the confinement concerned and the taking of blood samples for testing.

It is believed that congenital toxoplasmosis results from primary maternal infection during the period of gestation. Parasites disseminated through the body by the blood form small lesions in maternal tissues. Such a locus of infection in the placenta may infect the foetus. Beckett and Flynn (1953) have demonstrated the presence of parasites in a human placenta.

Congenital toxoplasmosis is stated not to occur in Tahiti (Feldman, 1956), where the infection is so prevalent that three-quarters of the population have acquired antibodies by the age of 9 (Feldman, 1953). This suggests that only people without antibodies are at risk, and that the presence of even a low titre of antibodies to the dye test indicates safety from blood-borne dissemination and consequent foetal infection.

Maternal infection in the first trimester of pregnancy is not invariably followed by foetal infection. Gard and Magnusson (1951), Stanton and Pinkerton (1953), and Holmdahl (1953) record instances of maternal infection at this stage which did not affect the foetus. Siim (1956) and Beckett and Flynn (1953), however, record cases of maternal lymphadenopathy in the third month of pregnancy followed by foetal infection, so even as early as this maternal infections are not devoid of risk. There is no record of maternal infection during the latter six months of pregnancy, in which the foetus was not affected. It is thought, however, that for stillbirth to result the infection must have taken place at least a month prior to delivery, and the most probable date for maternal infection would lie between eight months and one month before confinement. The interval between date of confinement and date of blood-sampling in this investigation ranged from 10 to 44 months. Thus if toxoplasmosis were responsible for any of these

foetal deaths the maternal infection must have taken place from 11 to 52 months before the serological investigations.

Serial dye test estimations on women who have borne affected children, cases of active toxoplasmosis, and women found to have high titres during an antenatal survey have been recorded by Holmdahl (1953), Feldman and Miller (1956), Makstenieks and Verlinde (1957), Beverley and Beattie (1958), Beattie (1958, 1960, personal communication), and others. From these it is apparent that after infection titres rise over a period of a few months to very high levels—of the order of 1/10,000—remain there for a short time and then fall. The fall is rapid at first and then becomes much slower, low titres persisting for many years. The rate of rise and fall is very variable. Titres of from 1/128 to 1/1,024 might be expected 11 months after infection, while four years after infection they would be between 1/16 and 1/256.

The excess of titres between 1/32 and 1/600 observed in the mothers of stillbirths in this series is therefore compatible with the theory that primary maternal infection took place during the period of gestation, and some of the stillbirths could therefore have been caused by toxoplasmosis.

All the serological tests were performed during the last four months of 1959. Consequently the interval between probable date of infection and the date of testing would be longest for the 1956 stillbirths and least for the 1958 cases, if toxoplasmosis were indeed responsible. This suggests a way in which the hypothesis may be tested, for if it were correct one would expect the titres for the 1956 cases to be the lowest and the 1958 cases to be highest. Because very recent infections give rise to extremely high titres, the use of an arithmetic mean would be misleading. An infection occurring subsequent to delivery in a woman whose stillbirth was due to some other cause would seriously affect this type of average. The median, however, is free from this form of bias.

As Table IX indicates, the median dye-test titres follow the pattern which one would expect if the theory that toxoplasmosis caused a proportion of the stillbirths were correct. It is impossible, in a retrospective investigation of this kind, to prove that toxoplasmosis was responsible for any particular stillbirth in the series. A statistical association such as this could result if toxoplasmosis and the true cause of the stillbirths were both related to a third factor, such as a common means of transmission. Nevertheless, the most probable explanation of the facts observed in this investigation is that toxoplasmosis was responsible for a proportion of the stillbirths. In assessing how many of the stillbirths may have been due to this cause, one must take into account the effect of the delay between confinement and blood-sampling as well as the differences in distribution of dye-test titre. If antibodies do in fact protect against infection there will be a greater risk of infection developing subsequent to confinement in the group with the higher proportion of negative dye-test reactors. Consequently a survey done some years after confinement may underestimate the differences between the two groups.

TABLE IX

Year of occurrence of stillbirth	1956	1957	1958
Median toxoplasma-dye-test titre	1 30	1 43	1/64

This appears to have occurred in this series, for a control mother whose baby was born in 1957 was found in December, 1959, to have a dye-test titre of 1/8,000. She gave a history of vague ill-health during the summer of 1959, which may have been related to her infection. Thus, though the excess of high titres in the stillbirth group is only 9, it is likely that a difference of 10 would have been observed had the tests been carried out a year earlier.

Since high titres fall rapidly and low titres persist for years, differences between two groups in incidence of high titres would be reduced by the passage of time even if no further infections occurred. For this reason also one would expect a survey undertaken some years after the confinements to underestimate the differences. It is therefore suggested that 10 of the 19 stillbirths may well have been caused by toxoplasma infection.

It will be seen from Table X that the distribution of dye-test titres in the control group does not differ greatly from what would be expected in a rural community on the basis of Professor Beattie's survey of blood donors in Lincolnshire (Beattie, 1957, 1959). The slight excess of positive reactors as compared with that expected in an urban community is in keeping with the theory that there may have been an epidemic of toxoplasmosis in Barton-on-Humber during the three years 1956–8. The controls appear likely to be representative of the community in respect of incidence of toxoplasma antibodies. Accepting this, it was found that even if only 11 instead of 13 of the mothers of stillbirths had shown positive dye tests at 1/32, the differences between the two groups would still have been significant at the 5% level ($\chi^2 = 3.96$). Thus it is unlikely that the number of stillbirths due to toxoplasmosis is lower than 3.

TABLE X

Test Titre	Expected* No.		Observed No. Barton
	Urban Rate	Rural Rate	Controls
Negative at 1/8	13	10	10
Positive at 1/8, negative at 1/16	2	2	3
,, ,, 1/16, ,, ,, 1/32	2	2	2
,, ,, 1/32, ,, ,, 1/64	1	3	3
,, ,, 1/64	1	2	1

* Derived by applying the rates observed by Beattie (1959) in blood donors in Lincolnshire to the number (19) of cases in survey and correcting to the nearest whole number.

In the past toxoplasmosis has not been regarded as a significant cause of stillbirths. None of the 633 stillbirths and neonatal deaths resulting from the 23,260 confinements investigated by Holmdahl (1953) in Goteborg between 1948 and 1951 showed evidence of toxoplasmosis, and only two cases of congenital disease were discovered. However, the perinatal mortality rate derived from Holmdahl's figures is only 27.2, compared with the figure of about 40 for England and Wales at that period. It would appear that Holmdahl was doing this work at a time when the disease was not prevalent in Goteborg. Such investigations in other areas, where the perinatal mortality rate is high, might well show a different result.

A more extensive investigation of all pregnancies occurring in the three districts of Lincolnshire during 1960 is at present in progress. It is hoped that this will prove whether toxoplasmosis is still a significant cause of stillbirths in the district. In addition, an attempt is being made to examine all the 300 children who were born in Barton-on-Humber during 1956–8, in order to

detect and treat any congenital infection. Confirmatory evidence that toxoplasmosis has been unusually prevalent in Barton-on-Humber may be obtained as a result of this work.

Conclusions

The most probable cause of the difference in incidence of stillbirths between the three districts of north Lincolnshire is infection with *Toxoplasma gondii*. Of the 19 stillbirths which occurred in Barton-on-Humber at least 3, and possibly as many as 10, are likely to have been due to toxoplasmosis. In only three cases could another cause for the stillbirth be definitely established, and the dye-test titres of two of these three mothers were among the three lowest titres observed in the series. The high incidence of malpresentation in Barton-on-Humber during this time could be due to toxoplasmosis, there being evidence in three out of the six breech presentations that the foetus was already dead or deformed prior to the onset of labour. If 10 of the 19 stillbirths were due to toxoplasmosis the remaining nine due to other causes would represent a rate of 28.2. This is still higher than the rates for England and Wales, but the difference is not significant.

Summary

Significant differences in perinatal mortality among three areas of Lincolnshire over a three year period are shown to be due to variation in stillbirth rate. Investigation of possible causes of this showed that there was a significantly higher incidence of cytoplasm-modifying antibody to *T. gondii* in the women whose babies had been stillborn, when compared with a group of mothers who had been delivered of live babies in the same month and in the same place. The two groups did not differ greatly in age, parity, or in any other respect. The hypothesis that toxoplasmosis may have been the cause of these stillbirths is discussed.

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REFERENCES

Bain, A. D., Bowie, J. H., Flint, W. F., Beverley, J. K. A., and Beattie, C. P. (1956). *J. Obstet. Gynaec. Brit. Emp.*, **63**, 826.
Beattie, C. P. (1957). *Trans. roy. Soc. trop. Med. Hyg.*, **51**, 96.
—— (1958). *Trans. Ophthal. Soc. U.K.*, **78**, 99.
—— (1959). Personal communication—giving more detailed information than appeared in Beattie (1957).
Beckett, R. S., and Flynn, F. J., jun. (1953). *New Engl. J. Med.*, **249**, 345.
Beverley, J. K. A., and Beattie, C. P. (1958). *Lancet*, **2**, 379.
Coffey, V. P., and Jessop, W. J. E. (1959). Ibid., **2**, 935.
Feldman, H. A. (1953). *Amer. J. trop. Med. Hyg.*, **2**, 420.
—— (1956). VIII int. Congr. Paediatrics, Copenhagen, 1956. Cited by Beattie (1957).
—— (1958). *Pediatrics*, **22**, 559.
—— and Miller, L. T. (1956). *Ann. N.Y. Acad. Sci.*, **64**, 180.
Gard, S., and Magnusson, J. H. (1951). *Acta med. scand.*, **141**, 59.
Holmdahl, S. C. (1953). *J. Obstet. Gynaec. Brit. Emp.*, **60**, 765.
McCreary, J. F. (1959). Lecture at Public Health Institute, Victoria, April, 1959. "The Child and His Environment." British Columbia Health Branch Department of Health Services and Hospital Insurance. P.H.S. Field Ref. File No. 6-1.
McDonald, A. D. (1958). *New Engl. J. Med.*, **258**, 767.
Makstenieks, O., and Verlinde, J. D. (1957.) *Docum. Med. geogr. trop. (Amst.)*, **9**, 213.
Nicolle, C., and Manceaux, L. (1908). *C.R. Acad. Sci. (Paris)*, **147**, 763.
Sabin, A. B. (1942). *Advanc. Pediat.*, **1**, 11.
Siim, J. C. (1956). *Ann. N.Y. Acad. Sci.*, **64**, 185.
Stanton, M. F., and Pinkerton, H. (1953). *Amer. J. clin. Path.*, **23**, 1199.
Wolf, A., Cowen, D., and Paige, B. (1939). *Science*, **89**, 226.

FULMINATING ULCERATIVE COLITIS

RECENT EXPERIENCE IN MANAGEMENT

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During the last few years new surgical and medical measures have become available for treating very severe acute episodes of ulcerative colitis. Some experience has now been gained in the use of these measures, and the time seems opportune for a review of some of the results obtained so that recommendations can be made for the future. We have studied the results of different treatments in a group of patients with very severe acute "fulminating" colitis and have tried to answer three questions: (*a*) Can treatment with corticotrophin or cortisone induce a remission in a "fulminating" episode of colitis? (*b*) When should surgical treatment be undertaken and what operation should be performed? (*c*) Does previous treatment with corticotrophin or steroid drugs influence the outcome of surgical treatment in these patients? Because "fulminating" episodes of colitis are uncommon and because the early years of treatment with steroid drugs have necessarily been exploratory, some of our conclusions can only be tentative, but from them we suggest a course of action for trial in the future.

Selection of Cases

Our aim has been to study a group of the most severe cases of ulcerative colitis seen at St. Mark's and the Central Middlesex Hospitals from 1951 to 1959. As we wished to select cases of acute colitis, we have not included in the series patients ill with serious metabolic disturbance, haemorrhage, or perforation of the colon, unless these complications were preceded by a severe exacerbation of the disease. Our selection has been made on account of the severity of the illness and without reference to the treatment given or its outcome. A definition of fulminating colitis has been impossible to achieve. No group of criteria adequately defines the severity of the illness. For example, neither fever nor tachycardia is adequate as a criterion, because three of our patients were critically ill with a high fever but a pulse rate less than 120 a minute, two were apparently overwhelmed by the illness with a pulse rate consistently above 150 a minute but with slight

fever, and several had a fever of 103–104° F. (39.4–40° C.) but have not been included in this series as they did not appear to be very ill.

In our selection we took account of fever, tachycardia, abdominal distension, mental changes, and biochemical disturbance, but eventually we came to rely mainly on the clinician's recorded impressions of the severity of the patient's illness and his memory of it as one that caused him great anxiety. Brooke (1956) has said that a fulminating episode of colitis "beggars exact definition," and suggested as criteria "severe toxaemia, pyrexia to 103–104° F. (39.4–40° C.), lethargy verging on coma, and serious alteration of blood chemistry." One or more of these criteria is present in 30 of our 32 cases.

The results of medical treatment described here cannot be regarded as representing the success rate among unselected cases of fulminating colitis, as several patients were transferred to the two hospitals when medical treatment elsewhere had failed.

Clinical Features of our Patients

The records of 520 patients admitted to St. Mark's and the Central Middlesex Hospitals for the treatment of ulcerative colitis during 1951 to 1959 have been examined and from them 32 patients have been selected for study.* Brief details of these patients are set out in Table I. In it our criteria for fever and tachycardia have been a temperature of more than 103° F. (39.4° C.) or a pulse rate of more than 120 a minute (any higher figure is shown) on four out of any seven consecutive days. The biochemical data show the most abnormal results during the illness. Clinical descriptions are taken as far as possible verbatim from the notes written at the time of the illness and are then enclosed in inverted commas. Where data are not available (as, for example, when a patient died within four days of admission) no entry is made in the Table.

*The proportion (6%) of patients selected accords well with the 10% of Brooke's (1956) surgical series and the proportion in other series, such as that of Crile and Thomas (1951).

Pathological Observations

A careful study made of the colon removed surgically at the height of the illness in 16 of our patients reveals features which explain some of the difficulties in the clinical management of this illness. Though mucosal ulceration was always very extensive, we were surprised to find that the mucosa of the caecum (and sometimes of the ascending colon also) was intact in 10 patients (Fig. 1) and that only in six was the whole colonic mucosa ulcerated; in all 16 the terminal ileum was normal. Histologically the wall of the colon showed grossly dilated blood-vessels and separation of muscle fibres by oedema. This intensely vascular base of the ulcers probably exudes fluid rich in protein, because the total serum protein was 4.5 g./100 ml. or less at one time in 7 out of the 17 of our patients in whom it was estimated; two of these patients (Cases 5 and 25) developed hypoproteinaemic oedema.

TABLE I.—*Clinical Details of the Patients (see Text for Explanation of Abbreviations). Patients are Numbered in the Order in which their Treatment is Described. Lines Separate Groups who Received Different Treatments*

Case No.	Age and Sex	Fever	Pulse	Abdominal Distension	Mental State	Serum Chemistry			Remarks
						Protein g./100 ml.	Na mEq/l.	K mEq/l.	
1	M 40	0	—	Moderate	Drowsy	4·0	114	4·1	"Acute toxic," gross loss of weight
2	F 33	0	150	Slight	Normal		125	4·8	Very weak, unable to move. Died
3	M 25	+	120	,,	,,	4·0	118	4·2	"An ill toxic patient"
4	M 48	0	150	,, 0	Drowsy	6·6	132	5·6	"Intensely toxic"
5	M 83	0	—	Moderate	Very drowsy	4·3	132	3·3	"Fulminating, acute." Gross oedema. Died
6	M 42	0	—	Slight	Drowsy		137	3·9	"A fulminating episode"
7	M 67	+	—	0	Drowsy. Confused	5·0	135	3·8	"Very toxic"
8	F 22	+	130	Moderate	Confused		137	3·7	"Typhoid state"
9	F 42	0	120	,,	Normal		135	4·7	"Toxic." Steady deterioration
10	M 31	0	120	,,	Confused	6·5			"Extremely ill"
11	F 34	+	120	0					"Very ill"
12	F 67	0	—	Slight	Normal				"Very ill indeed." Died
13	M 24	0	—	Moderate	Confused	5·0	98	5·2	"Most severe toxic state"
14	M 51	+	—	,,	Drowsy				"Going rapidly downhill"
15	F 30	0	—	,,	Normal				"Considerable toxicity." Increasing distension
16	F 19	0	120	Slight	Apathy		115	3·8	"Very toxic fulminating colitis"
17	F 32	+	120	Moderate	Normal	4·5			"Acute toxic state"
18	F 57	0	—	,,	,,		130	4·8	Emergency colectomy; increasing distension
19	F 40	+	120	0	,,	6·5			"More and more toxic"
20	F 28			Moderate	Confused				Emergency colectomy; distension and delirium
21	F 42	0	—	,,	Drowsy		137	4·8	"Intensely toxic." Died
22	M 32	+	—	0	Normal		141	5·5	"More and more toxic"
23	F 24	0	160	Slight	,,	5·4	118	3·5	"Overwhelming toxaemia, deteriorating steadily"
24	M 33	0	120	Moderate	Drowsy. Confused	5·8	122	3·8	"Ill and toxic." Died
25	M 44	0	130	Gross	Drowsy	3·5	123	2·3	"Very ill." Gross oedema. Died
26	M 28	+	120	0	Normal	5·4	115	4·3	"Critically ill." Died
27	F 27	+	120	Slight	,,	3·0	122	5·1	"Disease is rampant"
28	M 19	0	140	,,	,,	6·0	124	5·2	"Toxic; condition very poor." Died
29	F 30	+	120	0	,,		125	4·6	Emergency colectomy life-saving
30	F 22	+	120	Moderate	Drowsy		130	4·1	"Gravely ill"
31	M 42	0	130	Gross	Normal	5·5		5·2	"Extremely toxic." Died
32	M 51			0	Apathy	4·5			"Intensely toxic; profound apathy." Died

Not only were the ulcers large but they were also deep (Fig. 1), and penetration into the muscle coat was noted in 13 out of 16 patients. The inflammation had often spread through the muscle to involve the serosa, which was adherent to neighbouring structures in 10 out of the 27 patients who came to operation. This spread of inflammation into the muscle seems a likely

FIG. 1.—Case 14. Colon removed at operation, showing the contrast between the dilated right side of the colon with normal mucosa and the almost complete loss of mucosa with exposure of the circular muscle fibres on the left side. The ileum and caecum were normal both on inspection and on histological examination.

cause for the characteristic friability of the bowel wall in fulminating colitis. Extension of the ulceration into muscle was not necessarily associated with clinical abdominal distension in this series.

Results of Treatment

Cortisone and Corticotrophin

Seven patients were given a trial of cortisone or corticotrophin during a fulminating episode; three of them recovered without operation (Cases 4, 6, and 7).

Cases 1 and 2.—Both these patients were given cortisone, 200 mg. daily, without benefit.

Case 3.—This man was given corticotrophin, 120 units daily, for four days when he was admitted with two weeks' history of very severe colitis. As he improved only slightly, emergency ileostomy and subtotal colectomy was performed. At this operation the bowel was torn and his recovery was delayed by sepsis.

Case 4.—This patient did not apparently benefit from treatment with corticotrophin gel, 60 units daily, but later he slowly improved with general medical measures and was discharged well four months after admission.

Case 5.—A vigorous man of 83 had always enjoyed good health until the onset of severe colitis. Within five weeks he was grossly oedematous, without evidence of cardiac failure and with a low serum albumin of only 2 g./100 ml. Corticotrophin gel, 80 units daily, did not help him, and he died two weeks later.

Case 6.—This patient had had two milder episodes of colitis during the previous seven years. When admitted to hospital one month after a further exacerbation he was drowsy, had persecutory delusions, and was running a high fever. His condition did not alter while he was given corticotrophin gel, 80 units daily for three days, but when the dose was increased to 120 units daily there was a dramatic fall in temperature (Fig. 2) with a corresponding improvement in his well-being. He continued to improve, and was discharged free of symptoms after six weeks.

Case 7.—This patient had always been healthy until diarrhoea began abruptly, with the passage of three or four watery, often blood-stained, stools every hour. After three weeks of this he felt weak, lost his appetite, and began to vomit. He was admitted to hospital one week later a very ill man, wasted, dehydrated, and running a high fever (Fig. 2). Despite intravenous replacement therapy and chloramphenicol, his condition worsened over the next few days and he became drowsy and confused. Within a day of starting treatment with corticotrophin, 120 units daily, his mental state cleared and his temperature fell (Fig. 2). Three days later this note was made: "Has responded dramatically to corticotrophin, general condition now good, eating well and cheerful, less urgency of bowel action and no blood in stools." He continued to improve slowly and returned to work in normal health, passing one constipated stool each day, four months after his symptoms began.

Of the five patients who were given corticotrophin, two responded to a dose of 120 units daily. One of them did not respond to 80 units daily but did so to 120 units daily. Perhaps in fulminating colitis bigger doses of corticotrophin are needed than those in use at present.

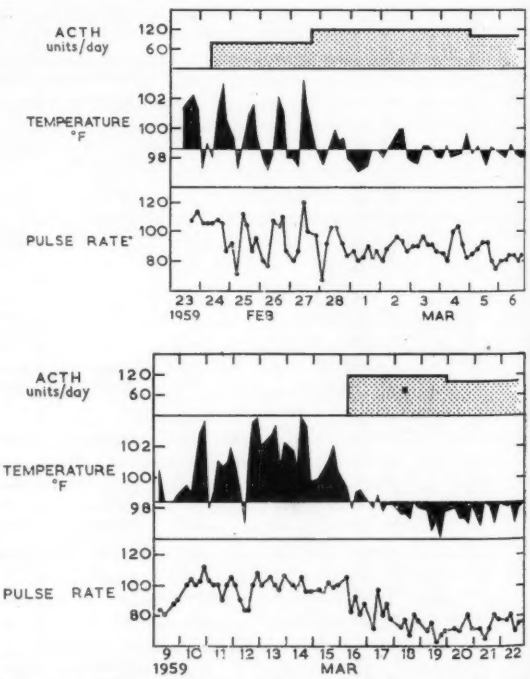

FIG. 2.—Temperature charts of Case 6 (above) and 7 (below), showing response to 120 units of corticotrophin daily and the lack of response to 80 units daily in Case 6.

Surgery Without Preliminary Corticotrophin or Steroid Drugs†

Opinion is divided on whether immediate colectomy and ileostomy should be performed or whether a preliminary ileostomy only should be undertaken, with subtotal colectomy as an elective operation later. Immediate colectomy with removal of the ulcerated inflamed bowel is the rational procedure, but there are powerful arguments against it; for instance, these patients are so ill that they may not be able to withstand such a major operation or the colon may be so fragile at the height of the illness that it tears when an attempt is made to remove it.

Preliminary ileostomy was performed four times in our series, each time because the surgeon favoured this policy. The results are set out in Table II. It will be seen that all the patients recovered and there was a satisfactory improvement in the general condition of two out of the four patients. Pathological examination showed that the colon was healing at the time of subsequent colectomy in every case, though in Case 10 the bowel was torn during mobilization; it may be significant that this colectomy was done only two weeks after the ileostomy.

Immediate colectomy was performed in 13 patients (Table III), of whom three died, four made a complicated recovery, and six recovered uneventfully. We think that at present these results must be considered satisfactory in this very severe disease. Could any of the deaths, however, have been avoided if ileostomy alone had been performed?

Case 21.—This patient, a woman aged 42, died after a severe rectal haemorrhage on the eighth post-operative day. Necropsy revealed bilateral bronchopneumonia and ulceration of the rectal mucosa but no bleeding-point.

We do not think that this death can be attributed to the colectomy; in fact, the portion of diseased bowel remaining caused her death.

Case 12.—A woman of 67 had had mild colitis for three years, and was admitted to another hospital with a very severe exacerbation. During the next five days she lapsed into stupor with high swinging fever and abdominal distension. She was transferred to St. Mark's Hospital for immediate operation, and subtotal colectomy with ileostomy was performed. A perforation of the caecum was found sealed to the sigmoid colon. For five days she improved slowly, but then her temperature rose and fatal circulatory collapse ensued. Necropsy revealed peritonitis.

Case 24.—This man, aged 33, was at work three weeks before he died, when a severe exacerbation of his proctosigmoiditis prostrated him. As his condition deteriorated during medical treatment, with a rising pulse rate and increasing lethargy, operation was decided upon. During the 36 hours before operation he became mentally confused and his abdomen became distended. At laparotomy the caecum and ileum were found to be greatly distended, the colon was acutely inflamed, and ascitic fluid was present. Subtotal colectomy was undertaken as it was feared that the colon might perforate spontaneously if ileostomy alone were performed; as it was, the colon was torn during mobilization. After operation his blood-pressure could not be maintained and he died 15 hours later. Necropsy revealed no local cause of death.

It is possible that these two patients might have been saved by a lesser operation, though the first was so ill that it is doubtful if any measure could have saved her. Despite careful observation the severity of the second patient's illness was underestimated and he was operated upon too late.

We cannot make a direct comparison between preliminary ileostomy and immediate colectomy because there are only four of the former in this series. These cases represent 4 out of 10 preliminary ileostomies performed as treatment for acute colitis at St. Mark's Hospital during the period 1951–9. The other six patients were severely ill, but not so ill as to be included in this series. The results of ileostomy in these cases were as follows:

Girl aged 18.—Continued deterioration. Immediate improvement after subtotal colectomy.

Man aged 61.—Excellent result. Uneventful colectomy.

Woman aged 56.—Continued deterioration. Died after proctocolectomy.

Woman aged 63.—Died after two days. Generalized peritonitis from perforation of sigmoid colon.

Man aged 66.—Satisfactory recovery, but complicated by pneumonia.

Man aged 20.—Continued deterioration. Colon torn at colectomy; died from intra-abdominal sepsis.

The poor results in these cases suggest that the results of ileostomy in our four patients were fortuitously favourable and that ileostomy alone cannot be relied upon to check the downhill course of severe colitis.

TABLE II.—*Results of Treatment with Ileostomy Followed by Colectomy in Patients who had not Received Treatment with Corticotrophin or Steroid Drugs*

Case No.	Post-operative Course	Interval until Colectomy	Colectomy	Time in Hospital after Ileostomy
8	Violent toxic psychosis for 3 weeks	15 weeks	Straightforward. Uneventful recovery	12 weeks
9	Good response. No complications	10 months	Colon adherent but removed intact. No complications	7 weeks
10	Acute delirium for 6 days	2 weeks (elective)	Colon torn at operation with subsequent pelvic abscess	9 weeks (including colectomy)
11	Good response. Ileostomy dysfunction	3 weeks (elective)	Straightforward. No complications	9 weeks (including colectomy)

TABLE III.—*Results of Immediate Colectomy in Patients who had not Received Treatment with Corticotrophin or Steroid Drugs*

Case No.	Adherent Colon	Colon Torn	Post-operative Course	Time from Operation to Discharge
12	Yes	? (Sealed pre-op. perforation)	Deteriorated after fair initial response. Died 7th day. Necropsy—peritonitis	
13	No	No	Confusional state for 4 weeks	8 weeks
14	,,	,,	Exacerbation of bronchitis	5 ,,
15	,,	,,	No complications	4 ,,
16	,,	,,	,, ,,	4 ,,
17	Yes	Yes (also pre-op. perforation)	Partial wound separation	7 ,,
18	No	No	No complications	4 ,,
19	,,	,,	,, ,,	13 weeks (includes rectal excision)
20	,,	,,	,, ,,	3 weeks
21	Yes	,,	Bronchopneumonia. Later massive rectal haemorrhage; died next day. Necropsy: bilateral bronchopneumonia	
22	No	,,	Burst abdomen	11 weeks (pan-proctocolectomy)
23	,,	,,	No complications	5 weeks
24	,,	Yes	Irreversible shock. Died	

†These patients were not given corticotrophin or steroid drugs for a variety of reasons; some were treated in the years before these drugs were commonly used, some were not given the drugs because they were so ill when admitted that it was thought dangerous to delay surgical treatment, and some because there were complicating factors such as healed pulmonary tuberculosis.

This lesser operation may be necessary because a patient's condition precludes more extensive surgery. It may be advisable if inspection at laparotomy suggests that the colon is especially apt to perforate during mobilization, owing to extensive adhesion to other structures or to fragility of its wall as a result of distension and inflammation. We consider that the results from immediate colectomy shown in Table III justify this as the operation of choice in most cases.

Does Treatment with Corticotrophin or Steroid Drugs Influence the Results of Surgical Treatment?

Of the eight patients who received these drugs during the three months before operation, four died and only two made an uncomplicated recovery. Why were the mortality and morbidity so high in this group? In considering this, we shall first present the results in the whole group (Table IV) and then discuss the fatal cases.

Table IV shows that the colon was torn during colectomy rather more often in this group than in the group (Table III) who had not received corticotrophin

TABLE IV.—*Results of Immediate Colectomy after Treatment During the Previous Three Months with Corticotrophin or Steroid Drugs*

Case No.	Length of Steroid Treatment	Adherent Colon	Colon Torn at Operation	Post-operative Course	Time from Operation to Discharge
1	16 days	Yes	No	No complications	4 weeks
2	9 ,,	Yes	Yes	Fatal circulatory collapse. Died	
3	5 ,,	No	,,	Pelvic abscess and wound sepsis	8 ,,
25	8 weeks	,,	No	Fatal circulatory collapse. Died	
26	10 ,,	Yes	,,	Subphrenic, pelvic, and intraperitoneal abscesses. Died	
27	5 ,,	No	Yes	Intra-abdominal abscesses and faecal fistula	6 months (colectomy and ileo-rectal anastomosis)
28	3 ,,	,,	No (pre-operative perforation)	Pelvic abscess, septicaemia, and pulmonary infarct. Died 25th day	
29	8 ,,	,,	No	No complications	4 weeks

or steroid drugs. We cannot correlate this occurrence with adherence of the colon to neighbouring structures, with the duration of steroid treatment, or with the length of the illness. There was one spontaneous perforation of the colon before operation in each group. This is in keeping with the findings of others that treatment with steroids does not increase the likelihood of spontaneous perforation of the bowel (Truelove and Witts, 1955; Goldgraber *et al.*, 1957).

Important lessons can be drawn from the fatal cases.

Case 2.—A woman aged 33 continued to deteriorate rapidly despite cortisone treatment. At the time of operation she was emaciated and weak, and a purpuric rash had appeared. The bowel was very adherent and was torn twice during mobilization, with gross peritoneal soiling. She collapsed immediately after operation and died five days later. The operation was not covered with cortisone.

Case 26.—A man aged 28 was critically ill, with a fever of 102–3° F. (38.9–39.5° C.), when he was transferred for operation after treatment with prednisone for 10 weeks. Subtotal colectomy and ileostomy was performed with cortisone cover, and, though there was no obvious soiling of the peritoneal cavity, subphrenic, pelvic, and intra-abdominal abscesses subsequently developed. In the interval before these were drained there was severe fluid and electrolyte disturbance (blood urea, 252 mg./100 ml.) due to the associated ileus. This was partially corrected (blood urea, 140 mg./100 ml.) before a second operation for draining the abscesses, which was not covered with cortisone. He died from circulatory collapse, unresponsive to intravenous hydrocortisone and noradrenaline, which developed two days later.

Both these patients had steadily deteriorated during medical treatment, and surgery was eventually undertaken as a last resort. This appears to have been the primary fault, but, in addition, both were operated upon without cortisone cover. At the time of the first patient's illness the need for extra cortisone at the time of operation was not yet appreciated. Beween his two operations the second patient presented a most difficult metabolic problem; so much attention was given to this that the need for cortisone cover at the second operation was overlooked.

Case 28.—A youth aged 19 began to deteriorate while being given cortisone, 200 mg. daily, and the physician decided that medical treatment had failed. Urgent operation was not undertaken, and spontaneous perforation of the caecum occurred four days later. Emergency subtotal colectomy and ileostomy was done, but subsequent intra-abdominal sepsis proved fatal.

This patient became worse while being treated with cortisone. The spontaneous perforation that occurred emphasizes the need for early operation if steroid treatment fails. During a period of medical treatment an initial sense of urgency may abate.

Case 25.—This patient was well for six weeks after a two-months course of corticotrophin. Profuse diarrhoea then began, and he was readmitted one week later with gross oedema (total serum protein 3.5 g./100 ml.), haemoconcentration (P.C.V. 54%), and hypokalaemia (2.7 mEq/l.). He improved with fluid and electrolyte replacement during the six days before his operation; there was then no evidence of haemoconcentration, his serum electrolytes were normal, but he was still grossly oedematous. He collapsed after uneventful subtotal colectomy and ileostomy. It seems unlikely that the collapse was due to cortisone lack, because he was given 200 mg. of hydrocortisone daily, beginning the day before operation.

This patient had gross oedema and a low serum protein; the problem was the same in Case 5. Fluid and electrolyte deficiencies were made good in both, but no vigorous attempt was made to replace protein, one of the most urgent needs in this type of case.

These results of the first few years of steroid treatment are disturbing, but results should be better in the future if some of these causes of failure are avoided.

Results in Miscellaneous Group

Case 30.—A woman aged 22 was admitted to hospital four weeks after her symptoms of colitis began. She was drowsy, her abdomen was distended, and she ran a fever of 103–4° F. (39.4–40° C.) for the first six days. Emergency colectomy was being considered, when spontaneous improvement began without specific treatment and she was discharged six weeks later in complete remission.

Case 31.—An emergency laparotomy was undertaken when this patient, a man aged 42, was admitted to hospital with a most unusual degree of abdominal distension and in a severely toxic state. On incising the peritoneum a grossly dilated and adherent transverse colon was accidentally opened; it was brought to the surface as a colostomy. An ileostomy was performed at a second operation but he died of peritonitis.

Case 32.—A man aged 51 was moribund when admitted to hospital and died before any treatment could be given.

Discussion

One in three of the patients whose cases are described died as a result of the illness. This startling fact requires analysis if the mortality is to be less in years to come. One patient (Case 32) was moribund when first seen. Of the rest it is important to emphasize that only 4 out of 31 patients were treated successfully by medical means alone; two of these successes can be attributed to corticotrophin. Only one patient (Case 5), aged 83, died without attempted surgical treatment; of the 26 patients operated upon, eight died (four of these without preliminary treatment with corticotrophin or steroid drugs). This mortality stands in marked contrast to the five deaths which occurred after 113 elective colectomies for ulcerative colitis at St. Mark's Hospital during the same period (Ewart and Lennard-Jones, 1960). In order to achieve better results, either operation must be avoided in the fulminating state or, if this is not possible, the patient must be in better condition when he is operated on; techniques which reduce the risk of perforation of the friable bowel at operation (Brooke, 1959) are also needed. A better medical regime might achieve remission in more patients. When a remission cannot be induced the emphasis must be on energetic metabolic replacement and early operation.

At present physicians perhaps have too much faith in corticotrophin or steroid drugs. The large-scale trial of cortisone in ulcerative colitis (Truelove and Witts, 1955) showed that this drug can induce a remission but does so less often in "severe" than in moderate or mild cases. Their criteria‡ for describing the illness as "severe" denoted patients who were ill but not as desperately ill as were those described here. It seems reasonable to suppose, therefore, that corticotrophin and steroids will be even less effective in a fulminating episode than in the more usual severe acute or chronic cases. Perhaps larger doses than at present usually given deserve cautious trial—for example, Cases 6 and 7—without placing too much reliance on this treatment. Kirsner *et al.* (1959) give 20–40 units of corticotrophin daily by intravenous infusion in fulminating colitis and up to 160 units daily by intramuscular injection in severe colitis. Since corticotrophin is more potent than cortisone in the treatment of relapses (Truelove and Witts, 1959) we suggest the use of this drug rather than cortisone for these critically ill patients.

If corticotrophin and steroid drugs are possibly given undue prominence, other measures may be receiving too little notice. Firstly, our analysis has emphasized the importance of replacing the protein and electrolytes which these patients have lost and are losing. Two of our patients (Cases 5 and 25) died mainly from metabolic depletion, particularly of the serum proteins, and in many others metabolic disturbance was obviously one very important cause of their prostration. When protein loss is severe, replacement with transfusions of whole blood and plasma (preferably drawn from a small panel of donors) would seem the best immediate treatment. Secondly, recent work has demonstrated a bacteraemia of portal-vein blood at elective colectomy for ulcerative colitis (Brooke and Slaney, 1958; Brooke, 1959) and a septicaemia in some patients after operation (Slaney and Brooke, 1958). It seems reasonable to take a blood culture from all patients with fulminating colitis, as some of them may have a septicaemia also. The general experience of broad-spectrum antibiotics in ulcerative colitis appears to be unfavourable, and 10 of our patients were given antibiotics without effect; clinicians are also rightly afraid of secondary infection of the bowel by drug-resistant staphylococci, as in the following case.

Case 23.—A woman aged 24 had been given tetracycline, 2 g. daily, as treatment for a severe exacerbation of colitis, but her condition had deteriorated steadily, so that when admitted to hospital she appeared overwhelmed by the illness, with a pulse rate persistently above 160 a minute. A severe pharyngitis was noted and throat swabs yielded a profuse growth of *Staph. pyogenes* resistant *in vitro* to tetracycline and penicillin, and only slightly sensitive to erythromycin. Stool culture yielded *Staph. pyogenes* of the same phage pattern, also insensitive to antibiotics; blood culture was sterile. Treatment with intravenous erythromycin was ineffective, but she made a rapid and uneventful recovery after subtotal colectomy. The operation specimen revealed confluent ulceration of almost the whole colonic mucosa.

Of the six patients who were given a course of insoluble sulphonamides, two probably benefited. We have no experience of salicylazosulphapyridine in the treatment of very severe colitis; Bargen (1955) does not recommend its use in fulminating colitis. As so many of the complications after colectomy were due to intra-abdominal sepsis, a trial of neomycin given pre-operatively seems worth while. Lastly, and just as important, Paulley (1956) and others have emphasized the value of dealing with the emotional upheavals found in many of these patients. It is clear that in this disease the physician must be prepared to give much time in getting to know the patients and their problems. He needs to gain their confidence, deliberately seek sources of emotional strain, and deal with the problems sympathetically as they arise, and actively support their morale more than in most other illnesses.

At present the indications for surgery are usually failure to improve during medical treatment, or the appearance of progressive abdominal distension, which is regarded as a sinister sign of impending perforation of the colon. In some of our cases—for example, No. 28—there was disaster because surgery was delayed. The operation of choice is still under discussion—a strong case has been made for preliminary ileostomy by Cattell (1953), but many surgeons now favour immediate colectomy (Aylett, 1959; Brooke, 1959; Goligher, 1959). We consider that the results presented here favour immediate colectomy but emphasize the dangers of perforation of the bowel during mobilization.

From our findings, some of which can only be tentative, we suggest a trial of the following scheme of management:

A Suggested Regime of Management for Trial

General.—The management of these patients is a matter for both physician and surgeon. As soon as the severity of the illness is recognized—and the severity is not always at once obvious—they should see the patient together and continue this close co-operation from day to day. A vigorous attempt should be made both to make good the metabolic depletion already present and to keep pace with further losses, not only of haemoglobin, fluid, and electrolytes, but also of protein. A blood culture is taken to detect a

‡Severe diarrhoea (six or seven motions a day) with macroscopic blood in stools. Fever (mean evening temperature more than 99.5° F. (37.5° C.), or a temperature of 100° F. (37.8° C.) or more on at least two days out of four). Tachycardia (mean pulse rate more than 90 a minute). Anaemia (haemoglobin 75% or less). E.S.R. much raised (more than 30 mm. in 1 hour).

septicaemia. It is important to gain the patient's confidence and to help with any emotional problems which may have precipitated the illness.

Corticotrophin.—(a) The patient has not received corticotrophin or steroid drugs: Give 120 units of corticotrophin daily for four days to test the response of the patient's illness to this drug, provided that delay in undertaking operation appears justifiable. *(b) Corticotrophin or steroid drugs have been given:* From a knowledge of the dose given a decision must be made whether these drugs received an adequate trial. If they did, corticotrophin should not be given; if not, a cautious trial of 120 units of corticotrophin daily for four days seems justifiable.

Indications for Surgical Treatment.—Unless operation is deliberately delayed for a trial of corticotrophin it should be performed as soon as the patient's obvious metabolic deficiencies have been met. Further delay is not permissible except when the disease appears to be going into remission after energetic general medical treatment. If a trial of corticotrophin is undertaken urgent operation is indicated if (*a*) there is no dramatic response to this drug and all other medical measures within four days; (*b*) the patient's condition deteriorates at any time during the treatment; or (*c*) after an initial successful response to corticotrophin a severe relapse occurs while he is still receiving the treatment.

Type of Operation.—We consider that the best procedure is immediate subtotal colectomy and ileostomy. If, however, the patient's general condition is desperate, or if inspection at laparotomy suggests that the colon is especially apt to perforate during mobilization, ileostomy alone may be preferable.

Summary

The results of treatment in 32 patients with very severe acute ulcerative colitis have been analysed.

The results of medical treatment were disappointing; one patient died without an attempt at surgical treatment, two patients responded to conservative measures, and two apparently responded to corticotrophin, 120 units daily (one of these patients did not respond to corticotrophin, 80 units daily).

Four patients were treated by ileostomy alone and all of them recovered. Reasons are given for supposing that these results were fortuitously favourable.

Twelve patients who had received no corticosteroid treatment were treated by immediate subtotal colectomy and ileostomy; three of them died and six made an uneventful recovery. It is suggested that this is the operation of choice in most cases.

Seven patients who had received corticosteroid therapy were treated by immediate subtotal colectomy and ileostomy; four of them died and two made an uneventful recovery. There was a dangerous deterioration in the condition of three of these patients during pre-operative medical treatment; two patients were not given extra cortisone at the time of operation. The colon was torn during colectomy rather more often among patients who had received corticosteroids than among those who had not received these drugs.

From our findings we suggest a possible regime for trial in the management of these very ill patients.

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REFERENCES

Aylett, S. (1959). *Postgrad. med. J.*, 35, 67.
Bargen, J. A. (1955). *Sth. med. J. (Bgham, Ala.)*, **48**, 192.
Brooke, B. N. (1956). *Lancet*, **2**, 532.
—— (1959). Ibid., **2**, 745.
—— and Slaney, G. (1958). Ibid., **1**, 1206.
Cattell, R. B. (1953). *Proc. roy. Soc. Med.*, **46**, 1021.
Crile, G., and Thomas, C. Y. (1951). *Gastroenterology*, **19**, 58.
Ewart, W. B., and Lennard-Jones, J. E. (1960). *Lancet*. In press.
Goldgraber, M. B., Kirsner, J. B., and Palmer, W. L. (1957). *Gastroenterology*, **33**, 434.
Goligher, J. C. (1959). *Scot. med. J.*, **4**, 1.
Kirsner, J. B., Palmer, W. L., Spencer, Jean A., Bicks, R. O., and Johnson, C. F. (1959). *Ann. intern. Med.*, **50**, 891.
Paulley, J. W. (1956). *Lancet*, **2**, 215.
Slaney, G., and Brooke, B. N. (1958). Ibid., **1**, 504.
Truelove, S. C., and Witts, L. J. (1955). *Brit. med. J.*, **2**, 1041.
—— —— (1959). Ibid., **1**, 387.

LOCAL CORTICOSTEROID TREATMENT IN SEVERE ATTACKS OF ULCERATIVE COLITIS

BY

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Since 1955 considerable experience has been acquired in the use of corticosteroid solutions applied locally within the colon by means of a rectal drip for the treatment of ulcerative colitis. The initial studies showed that mild and moderate attacks were often checked abruptly, so that the patient became symptom-free in a few days, though a minority of attacks failed to respond (Truelove, 1956, 1957). A special feature of these early studies was that the water-soluble corticosteroid, hydrocortisone hemisuccinate sodium, was shown by serial biopsy of the mucosa to produce striking histological improvement in those patients showing a favourable symptomatic response. Consequently this agent, or another water-soluble corticosteroid, prednisolone 21-phosphate, has since been the agent of choice for this form of treatment.

Since these early studies, local corticosteroid treatment has been tested in two independent controlled therapeutic trials, carried out in Oxford and Leeds respectively, both of which were conducted on the so-called "double-blind" system with neither the physician nor the patient knowing whether a particular treatment was corticosteroid or "dummy." Both studies yielded convincing evidence that local corticosteroid treatment usually caused a rapid cessation of mild and moderate attacks of ulcerative colitis, whereas it was exceptional for a patient to undergo spontaneous loss of symptoms when given the dummy treatment (Truelove, 1958; Watkinson, 1958). Subsequently it has been found that local corticosteroid treatment is twice as likely to bring about a rapid clinical remission as a comparable dose of corticosteroid given by mouth, but that it is even more efficient to use combined systemic and local corticosteroid therapy consisting of prednisolone by mouth and hydrocortisone hemisuccinate sodium by rectal drip (Truelove, 1960).

All these published studies were concerned with the value of local corticosteroid therapy in mild or moderate attacks of ulcerative colitis, and it has sometimes been assumed that this form of treatment is useful only in such attacks and has little or no place in the management of a severe attack. In reality, local

corticosteroid treatment has been used in Oxford in the medical management of severe attacks of ulcerative colitis ever since the first study on the lesser attacks had suggested that this form of treatment was beneficial. Sufficient experience has now been obtained to warrant the conclusion that this form of therapy represents an advance in treatment for severe attacks as well as for mild or moderate ones.

The present article consists of three main sections. First, some illustrative case-histories are given to demonstrate some of the results obtained in individual cases and some of the practical problems entailed in this form of treatment. Secondly, based on experience of these and many other in-patients, a scheme for the medical management of severe attacks is formulated. Thirdly, some consideration is given to the evidence supporting the view that local corticosteroid therapy is beneficial in severe ulcerative colitis.

Case 1. Severe Attack Complicated by Massive Bleeding from Bowel

A married woman aged 33 was admitted to hospital on July 26, 1957, in a severe attack of ulcerative colitis. Two months before admission diarrhoea occurred, with up to 10 bowel actions daily and with bright blood in the faeces. There was lower abdominal pain and tenesmus. Four weeks before admission she developed anorexia, flatulence, and increasing weakness, while the diarrhoea became more severe and there was blood intimately mixed in the motions.

Past History.—Pulmonary tuberculosis had been discovered after her third pregnancy and had been treated with satisfactory results.

Family and Social History.—There was an extremely unstable background with an aggressive psychopathic husband. The family was in considerable financial difficulties, and one of the three children was being cared for in an institution because of lack of attention at home.

On admission she was a pale, emaciated, and anxious woman with fever and tachycardia, the temperature being 103° F. (39.4° C.) and the pulse rate 110 a minute. There were numerous aphthous ulcers in the mouth. The cardiovascular system showed a simple tachycardia with a blood-pressure of 95/65 but no other abnormalities. The abdomen showed tenderness in the left iliac fossa but no other abnormality.

Investigations on Admission.—Blood: haemoglobin, 60% (9.2 g./100 ml.); white cells, 8,100/c.mm.; film showed iron-deficiency changes; E.S.R., 86 mm. in one hour. Blood chemistry: some degree of hypokalaemia (serum potassium, 3.4 mEq/l.) and hypoalbuminaemia (albumin 3.1 g./100 ml.). Chest *x*-ray examination showed "minimal residual lesion in right second interspace." Stools: numerous red blood cells but no parasites, ova, or acid-fast bacilli; culture showed no pathogenic organisms. Barium enema: "Ulcerative colitis affecting the entire colon." Sigmoidoscopy showed "severe inflammation with a haemorrhagic mucosa which oozes blood freely."

Treatment and Progress

She was admitted to a large-scale trial of cortisone and corticotrophin therapy which was then in progress and was allotted to cortisone, which was given in a dose of 50 mg. four times a day. During the first three weeks of this treatment she had recurrent episodes of severe bleeding, each of them necessitating urgent blood transfusion. In the fourth week a severe abdominal episode occurred which was thought to be a small perforation of the colon with walling off of a localized abscess in the left iliac fossa. Cortisone was temporarily discontinued and terramycin and further blood transfusions were given. She resumed cortisone until the six-weeks trial period was completed; treatment was then changed to corticotrophin gel in a dose of 80 units daily. After treatment with corticotrophin for one week she developed a severe urinary infection and diabetic precoma, with a blood-sugar of 550 mg./100 ml. and associated severe electrolyte disturbances of the blood. Corticosteroid therapy was stopped and general medical measures were taken, and insulin was given for the diabetic state. However, after another week further heavy bleeding from the bowel necessitated immediate transfusion of six bottles of blood.

At this point she was a severely ill woman with high fever and low weight (5 st.: 32 kg.). Emergency colectomy was contemplated, but was thought to be undesirable if it could possibly be avoided because of the unsatisfactory social background which would have fitted in badly with a permanent ileostomy life. It was therefore decided to try the effect of local hydrocortisone treatment, and a rectal drip of hydrocortisone hemisuccinate sodium was given three times a day together with 5 mg. of oral prednisolone four times a day. In a few days there was a marked improvement. Further blood transfusion was not needed, though she had previously received more than 60 bottles of blood (30 litres). The temperature, which was running at up to 105° F. (40.6° C.), settled to normal. Blood diminished in the stools and became absent, and she began to gain weight. Thereafter progress was uneventful, and when discharged from hospital she was having one or two normal motions a day and her weight had risen to 8½ st. (54 kg.).

Long-term Progress.—After discharge from hospital all treatment was discontinued, and she remained well until February 22, 1958. Then, while shopping in Oxford, she was suddenly seized with abdominal pain and went to a public lavatory, where she passed large amounts of blood per rectum. She came to the casualty department of the Radcliffe Infirmary, and I saw her sitting on a bedpan passing almost pure blood from the bowel. She was admitted, given a blood transfusion, and put on to a rectal drip of hydrocortisone hemisuccinate. This was well retained from the start. By the next morning there was no fresh blood in the faeces, and three days later blood was completely absent. She was discharged one week after admission with one normal motion a day, to continue on the daily rectal drip at home. Since that time she has been kept under regular observation. For one period she has needed treatment with the combination of oral prednisolone and the rectal drip of hydrocortisone, but otherwise has been well. Since December, 1958, she has received no treatment and has been symptom-free. At the time of writing the sigmoidoscopic and the barium-enema appearances were normal.

Comment.—The severe first attack of the disease resisted treatment by general medical measures coupled with oral cortisone at first and later with intramuscular corticotrophin. Throughout she was liable to recurrent episodes of severe haemorrhage from the bowel. When systemic corticosteroids were stopped for a week, she continued to have severe ulcerative colitis and had a further severe haemorrhage. The institution of local hydrocortisone hemisuccinate therapy at this point, coupled with a comparatively small dose of oral prednisolone, was followed by rapid improvement and uneventful recovery. The long-term course has so far proved satisfactory and the bowel has reverted to normal as judged by sigmoidoscopy and barium-enema appearances.

Case 2. Severe Relapse Responding Rapidly to Local Hydrocortisone

A transport driver aged 31 was admitted to hospital in a severe relapse of ulcerative colitis on November 15, 1957. In 1946 he had an attack of diarrhoea with some blood in the motions while serving in the Army in India, this illness being labelled as "dysentery." Since that time he has been liable to attacks of diarrhoea with blood and mucus in the stools, and ulcerative colitis was diagnosed at the Radcliffe Infirmary in 1947. In August, 1956, he suffered from a

sharp relapse which was treated in hospital for two months with systemic prednisolone. Thereafter he was relatively well with about four motions a day until September, 1957, when there was a sharp relapse with 25–30 stools daily. He had severe abdominal pain during and after defaecation and tenesmus. He lost weight rapidly and was admitted to hospital.

On admission he was a thin, ill-looking man with fever, the temperature being 100° F. (37.8° C.). In the abdomen there was marked tenderness over the descending and iliac colon.

Investigations.—Blood: haemoglobin 94%; white cells, 27,000/c.mm.; E.S.R., 62 mm. in one hour. Blood chemistry was satisfactory. Barium enema: "severe ulceration affecting the whole of the colon." Sigmoidoscopy: appearances of severe ulcerative colitis.

Treatment and Progress

For the first week he was treated with general medical measures, but he continued to deteriorate rapidly with painful motions every half-hour and loss of nearly 1 st. (6.4 kg.) in weight. At this point he was treated with local hydrocortisone, which was used somewhat differently from the method employed in Case 1. A large quantity of hydrocortisone—namely, 400 mg. of the hemisuccinate—was dissolved in 1 pint (500 ml.) of normal saline and was run rapidly into the bowel each night after a preliminary intravenous injection of 30 mg. of propantheline bromide ("probanthine"). The intention was to ensure that the hydrocortisone travelled throughout the whole colon. In addition to this treatment he was given penicillin, 1 mega unit twice daily, and streptomycin, 1 g. twice daily, both by intramuscular injection. On this regime he rapidly went into remission. His bowel habit rapidly showed improvement, and both the white blood count and the E.S.R. fell swiftly to normal values. The one complicating feature was the development of anorexia and nausea, which were attributed to the effect of probanthine; these symptoms disappeared when the dose was reduced to 15 mg. He was discharged from hospital on January 6, 1958, treating himself with a nightly rectal drip of 100 mg. of hydrocortisone hemisuccinate in 150 ml. of saline.

Long-term Progress.—Since that time he has been kept under supervision as an out-patient. He has had one further relapse of ulcerative colitis, but this was rapidly checked by treating him as an out-patient with a combination of 5 mg. of prednisolone by mouth four times a day and a nightly rectal drip of 100 mg. of hydrocortisone hemisuccinate sodium. For the past year he has had no treatment and the sigmoidoscopic appearances were normal, while a recent barium-enema examination has been reported on as follows: "The examination shows a remarkable improvement in the colon, all parts of which show a smooth outline. The distal colon is devoid of haustrations, but after the enema there was a good evacuation and the colon contracted well" (Dr. K. Lumsden).

Comment.—A severe relapse of established ulcerative colitis responded to local hydrocortisone used in a particular way. A large quantity of hydrocortisone was employed in 1 pint (500 ml.) of saline after a preliminary intravenous injection of propantheline bromide to paralyse the gastro-intestinal tract and thus increase the chance of the hydrocortisone being retained in the colon. The response was good, but the method of administration is somewhat troublesome for the physicians concerned.

Case 3. Severe Relapse Treated with Systemic Triamcinolone and Local Hydrocortisone Hemisuccinate Sodium

A married woman aged 47 was admitted to hospital as an emergency case on August 18, 1958. There was a history of ulcerative colitis extending over the past 22 years, the first attack occurring with her first pregnancy. Since that time she has been liable to attacks of the disease, but was completely well between attacks. The last previous attack was in 1956, when she spent 17 weeks in a London teaching hospital and was severely ill. On the present occasion bloody diarrhoea had begun two weeks before admission and had become severe.

On admission she was a flushed middle-aged woman with a fever, the temperature being 102.4° F. (39.1° C.), and with tachycardia, the pulse rate being 100. The abdomen was slightly distended and there was tenderness over the descending colon.

Investigations on Admission.—Blood: haemoglobin 105% (15.2 g./100 ml.); white cells, 9,000/c.mm.; E.S.R., 36 mm. in one hour. Faeces: culture showed no pathogenic organisms. Barium enema: "extensive changes of ulcerative colitis involving the rectum, sigmoid, and descending colon, and the distal half of the transverse colon."

Treatment and Progress.—She was treated with systemic steroids, at first hydrocortisone intravenously and then triamcinolone orally in a dose of 8 mg. four times a day. Rectal drips of hydrocortisone hemisuccinate sodium, 100 mg. were given twice a day, together with propantheline bromide intravenously before the evening drip in order to keep the hydrocortisone in place. Improvement was rapid and normal stools were passed after one week. She was discharged on September 1, 1958, two weeks after admission, to continue treatment with rectal hydrocortisone at home. Treatment was continued on an out-patient basis until November, 1958, when it was stopped. Thereafter she remained well until February, 1959, when there was a recurrence. She was treated as an out-patient with triamcinolone, 4 mg. four times a day, by mouth, and a nightly rectal drip of hydrocortisone hemisuccinate, and showed a rapid response. Since that time she has remained well.

Comment.—This case-history illustrates the prompt response to combined local and systemic corticosteroid treatment which is shown by many patients.

Case 4. Sharp Relapse Complicated by Arthritis

A married woman aged 36 was admitted to hospital on July 31, 1958, because of ulcerative colitis. She developed the condition in 1939, when she was ill for 10 months; the diagnosis was confirmed by barium enema. There were recurrences in 1947, 1957, and 1958. In the 1958 attack she was treated with rectal hydrocortisone for three weeks and did well. Thereafter she remained well until six weeks before the present admission, when diarrhoea suddenly developed with 10 watery motions a day. She was treated as an out-patient with a rectal drip of hydrocortisone and improved, but then stopped it. The diarrhoea became worse, and severe pains developed in the left ankle, left calf, left shoulder, neck, and the right arm.

On admission she was moderately ill, with fever, the temperature being 101° F. (38.3° C.), and tachycardia, the pulse rate being 120. The neck was very painful on movement, and several other joints were also painful, though there was little to find on objective examination.

Investigations.—Blood: haemoglobin 82%; white cells, 14,200/c.mm. Blood chemistry: mild hypokalaemia (serum potassium, 3.7 mEq/l.).

Treatment and Progress.—After five days in hospital without benefit from general medical treatment she was given a combination of prednisolone by mouth in a dose of 10 mg. four times a day and a rectal drip of hydrocortisone twice daily. Because of severe aphthous ulceration prednisolone phosphate was prescribed as a mouth-wash. With this treatment she rapidly improved, becoming almost normal after three days. The temperature, which had continued to show an evening rise to 101–102° F. (38.3–38.9° C.) each day after admission, remained normal from

the start of this treatment. She was discharged after two weeks' treatment. Since that time she has remained well.

Comment.—Both arthritis and severe ulceration of the mouth are common complications of ulcerative colitis. When the colitis is treated successfully, whether by medical treatment or by colectomy, both these complications disappear. In this particular case treatment with corticosteroids was rapidly effective.

Case 5. A First Attack Presenting as a Sudden Haemorrhage from the Bowel

A married woman aged 58 was admitted to hospital on April 16, 1958, as a surgical emergency because of heavy bleeding from the bowel. Two days before admission she suffered from severe intermittent abdominal pain with vomiting, these symptoms persisting until admission. On the day before admission she developed diarrhoea and passed a small quantity of blood. On the day of admission large quantities of blood were passed per rectum. The provisional diagnosis on admission was acute diverticulitis with massive bleeding. However, the house-surgeon observed that faecal material was intimately mixed with the blood passed per rectum, and the possibility of ulcerative colitis occurred to him. It was arranged for me to carry out sigmoidoscopy without delay, and this showed that the entire mucosa of the rectum and lower sigmoid colon, as far as could be seen, was hyperaemic and oedematous, with marked contact-bleeding. The appearances were those of ulcerative colitis. A barium-enema examination one day later revealed multiple irregularities of the outline of the sigmoid and descending colon, suggesting ulcerative colitis.

Treatment and Progress.—Three pints (1.5 litres) of blood were transfused immediately. She continued to pass large amounts of blood per rectum until the day after her admission, when sigmoidoscopy showed the condition to be ulcerative colitis. She was then put on a rectal drip of hydrocortisone hemisuccinate, and thereafter had no further bleeding and the stools became normal. The bowels were not opened for three days after the first rectal drip. Seven days after starting the rectal drip repeat sigmoidoscopy showed only slight inflammation. She was kept under supervision as an out-patient. The nightly use of a rectal drip of hydrocortisone hemisuccinate was continued for some weeks after discharge from hospital; she was then entirely normal symptomatically and the sigmoidoscopic appearances were likewise normal. A repeat barium enema also showed normal appearances. She has remained entirely well since.

Comment.—My previous experience has been that patients who begin with heavy bleeding from the bowel usually suffer from a severe attack of ulcerative colitis. In this particular case the bleeding was immediately stopped by the use of local hydrocortisone hemisuccinate, with reversion of the bowel to entire normality so far as can be judged by our present methods of study.

Scheme for the Medical Management of a Severe Attack of Ulcerative Colitis

A severe attack of ulcerative colitis demands urgent admission to hospital and the immediate institution of certain general medical measures which are applicable to the treatment of any case of severe bloody diarrhoea, no matter how caused. As soon as the diagnosis is made, which is usually not difficult in a severe attack of this disease, the other measures which are employed to shorten the attack should be brought into play.

General Medical Measures

1. *Correction of Dehydration and Electrolyte Depletion.*—Whenever there is profuse diarrhoea there is heavy loss of water and of electrolytes. In particular the loss of potassium may be heavy, and the patient may be rendered gravely ill on this account alone. It is sometimes possible to correct electrolyte deficiencies by the oral administration of appropriate replacement fluids, but if there is vomiting or the electrolyte disturbance is severe it is best to employ intravenous infusion. Once corrected, regular biochemical observations should be made while the illness is in a severe stage, so that corrective measures can be reinstituted whenever necessary.

2. *Blood transfusion, to be repeated as often as necessary,* should be carried out to maintain the haemoglobin at a high level. In other words, the blood which is being lost per rectum is replaced without the body having to call upon its own stores of protein to make good the loss. In severe ulcerative colitis there is heavy loss of nitrogen from the bowel, so that any measure which spares the protein stores of the body is valuable in preventing rapid wasting.

3. *A high calorie intake,* preferably with a large amount of protein, should be instituted. This is sometimes impossible at first, because vomiting and anorexia are common features of an acute attack. In such circumstances glucose should be added to the intravenous infusions, and the measures designed to cut short the attack will usually restore the appetite in a few days.

4. *Vitamin supplements* should be administered, because deficiencies can occur in the course of the disease. Vitamin B complex should be given parenterally, especially if antibiotics are being used. Folic acid and vitamin B_{12} are possibly worth giving if a severe attack lasts for more than a week or two. There is no convincing evidence that they do much good, but their use is harmless.

Specific Agents Used to Cut Short the Attack

Two main types of therapeutic agent have been extensively used in recent years because they appear to cut short the attack. They are salicylazosulphapyridine ("salazopyrin") and corticosteroid therapy. Salazopyrin is a Swedish preparation which was introduced in 1940 by Svartz and has since been much used in the treatment of ulcerative colitis. In Oxford we have not made extensive use of this agent in the treatment of severe attacks of the disease, such as are now being discussed, but those who are interested will find references to its use in a number of articles (Svartz, 1942, 1948, 1954, 1956; Lagercrantz, 1949, 1955; Bargen, 1955; Morrison, 1952, 1953; Spriggs *et al.*, 1958).

Corticosteroid therapy has been our mainstay in Oxford for cutting short attacks of ulcerative colitis. There are two distinct ways of using corticosteroid therapy—namely, systemically or by local application to the colon. Our general experience is that it is best to combine these two methods for the treatment of a severe attack. Certainly in the less severe attacks it has been shown that the combined use of systemic and local corticosteroid therapy is more efficient in producing rapid clinical remission than either method used alone (Truelove, 1960). It is reasonable to assume that the same general principle holds good in the treatment of a severe attack of the disease, though we employ higher dosage than in the lesser attacks. Nowadays we employ one of the newer analogues of cortisone for systemic therapy, and prednisolone by mouth in an initial dose of 15 mg. four times a day appears to be generally satisfactory, though triamcinolone and dexamethasone have also been used in some cases. When the attack is exceptionally severe, and especially if there is much nausea and vomiting, it is convenient to begin systemic corticosteroid therapy by giving intravenous injections.

We originally gave hydrocortisone hemisuccinate sodium in doses of 100 mg. twice a day, but more recently have used prednisolone 21-phosphate 25 mg. twice a day. Prednisolone phosphate enjoys an advantage over hydrocortisone hemisuccinate in having less effect on electrolytes, so that the control of electrolyte metabolism is easier. In addition, a comparative study of various forms of corticosteroid treatment in the less severe attacks of ulcerative

colitis has shown that the combination of systemic prednisolone and local hydrocortisone is a highly effective approach (Truelove, 1960).

At the same time that systemic corticosteroids are being used, local hydrocortisone hemisuccinate is administered by rectal drip twice a day. Before the evening rectal drip it is usual to give at the height of the attack an intravenous injection of propantheline bromide in a dose of 30 mg. for an adult in order to paralyse the gastro-intestinal tract and thus facilitate the retention of the local hydrocortisone within the colon. It is usual to employ 100 mg. of hydrocortisone dissolved in approximately 150 ml. of saline for each rectal drip, though on occasion we have used larger quantities of hydrocortisone dissolved in a much bigger volume of saline, as described in Case 2 above. It is not yet certain which is the better of these two methods of using hydrocortisone locally, but the large-volume method demands the presence of a physician and is therefore more troublesome. Radiological studies that have been made using barium suspensions on lesser attacks of the disease have shown that the bigger volumes travel further in the colon and can always be relied upon to reach the ascending colon, but similar studies have not yet been made in patients actually suffering from a severe attack.

A word of caution must be interpolated about the use of intravenous propantheline. When it is used nightly, as described above, it is essential that neither propantheline nor any other anticholinergic agent be given by mouth in addition, if overdosage is to be avoided. Even when using a nightly dose of 30 mg. intravenously on its own we have in a few patients encountered evidence of overdosage, which has shown itself as abdominal distension, anorexia, nausea, and tachycardia, with a general picture resembling that of a paralytic ileus. It is important to keep this cause of abdominal distension in mind, because abdominal distension can occur in ulcerative colitis from other causes, notably from potassium depletion or from a perforation of the colon, which, if small, may not be clinically obvious, especially if corticosteroids are being used in treatment. If signs of overdosage of propantheline appear, the dose should be reduced or this treatment stopped for a day or two.

Accessory Measures

Antibiotics and sulphonamides have a secondary but important role in the treatment of acute attacks. They minimize the chance of developing a pyogenic complication of the disease, and this is particularly important when corticosteroid therapy is being employed at full dosage. Penicillin has the virtue of negligible toxicity, but is effective against a limited range of organisms. The combined use of penicillin and streptomycin by intramuscular injection appears to be a good method of combating the risk of pyogenic complications in severe cases, but streptomycin should not be continued for more than about a week. The broad-spectrum antibiotics should not, in my opinion, be given by mouth in this disease, because they are themselves liable to create a dangerous enterocolitis. When broad-spectrum antibiotics are used it is best to choose one which can be given parenterally and to keep to a short course of treatment. It has now become usual for us to employ intravenous achromycin or terramycin for a few days at the beginning of a treatment of a severe attack when there is much fever present.

It will be appreciated that the foregoing scheme is a provisional one which may have to be altered as new developments in corticosteroid therapy occur. In addition, it is designed for the treatment of an uncomplicated attack of ulcerative colitis. Certain complications demand emergency surgery, perforation of the colon being the outstanding example. Other complications of the acute attack are often improved by treating the colitis along the lines covered, but there are exceptions. A notable one is when moniliasis of the mouth develops, because there is evidence that both broad-spectrum antibiotics and systemic corticosteroid therapy are apt to cause a spread of moniliasis which may affect the entire gastrointestinal system or the respiratory system. When moniliasis develops, it is usually best to stop temporarily the use of broad-spectrum antibiotics and systemic corticosteroids and to employ nystatin tablets for local and systemic treatment until the fungous infection has come under control.

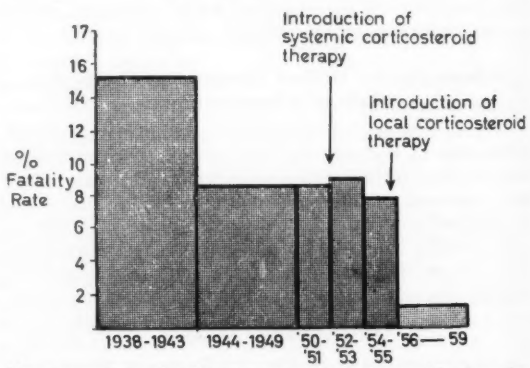
Evidence that Local Corticosteroid Treatment is Beneficial

The presentation of a group of favourable case reports, such as those given above, cannot be regarded as entirely adequate evidence that local hydrocortisone has been a beneficial addition to the medical management of a severe attack of ulcerative colitis. Any physician with an extensive experience of this disease can assemble a group of patients who made a dramatic response to medical treatment before corticosteroid therapy was introduced. It is therefore necessary to take a much more general view of the results than can be obtained from isolated case histories.

Number of Deaths from Ulcerative Colitis in Radcliffe Infirmary and Churchill Hospital During the Period 1938–59 *Inclusive (multiple admissions of the same patient in any one year are counted as a single patient being admitted)*

	No. of Admissions	Deaths in Hospital	
		No.	%
1938–43 ..	78	12	15·4
1944–49 ..	151	13	8·6
1950–51 ..	59	5	8·5
1952–53 ..	78	7	9·0
1954–55 ..	82	6	7·3
1956–57 ..	105	1	0·95
1958–59 ..	103	2	1·9

The Table and Chart show the case-fatality rate of in-patients with ulcerative colitis treated in the Radcliffe Infirmary and Churchill Hospital since 1938, when the medical records were put on to a modern system. Patients who were admitted more than once in the same year are counted as a single case for that year, but a similar picture would be obtained if the Table and Chart were presented in the form of fatality rate per 100 admissions, though the rate would be somewhat lower throughout. It will be seen that during the first six years of the period under review, 1938–43 inclusive, no less than 15% of the patients admitted to hospital died in hospital. Then, at the end of the war, the rate fell to approximately 8%. It is probable that this drop



Mean annual case-fatality rate among in-patients with ulcerative colitis treated in the Radcliffe Infirmary and Churchill Hospital, Oxford.

represented an improvement in general medical care and in particular the full realization of the importance of electrolyte control in the severe attacks.

From 1944 onwards the fatality rate did not differ much from 8% until 1956, though the use of systemic corticosteroids began in 1952 and were widely used by 1954, when the results of a controlled trial showing that they were beneficial were available (Truelove and Witts, 1954). The six-year period 1950–5 has been broken down into three two-year periods to show that the rate remained remarkably steady throughout. Local hydrocortisone treatment began to be used in Oxford in 1955 and was applied to the treatment of severe attacks from 1956 onwards. It can be seen that since that time there has been a sharp fall in the case-fatality rate from ulcerative colitis among in-patients, the rate now being approximately 1.5%. This level represents the death of three patients during the four-year period 1956–9 inclusive.

The first of these deaths occurred in an elderly man with long-established ulcerative colitis who died a few days after admission to hospital from a large pulmonary embolism secondary to a silent leg-vein thrombosis which he had presumably developed at home before admission. The second death was in an elderly woman who first came to the Radcliffe Infirmary in 1957 with a history of ulcerative colitis since 1942, untreated except in the first attack; a carcinoma of the sigmoid colon was present, and she was treated by colectomy and ileostomy. Thereafter she had episodes of obstructive symptoms, causing her to be readmitted for exploration in 1958, when intra-abdominal metastases were found. She subsequently died from ileal perforation and peritonitis. The third death was in a severe first attack of the disease occurring in a man who suffered also from the haemorrhagic condition Christmas disease; in him it was impossible to stop massive haemorrhage from the bowel, so that, after 80 bottles of blood had been transfused in the course of a few weeks, surgery became imperative as a final attempt to save his life, but without avail. There have been no deaths from uncomplicated ulcerative colitis during the period—a considerable change from earlier years.

In assessing the value to be attached to these figures, certain other facts must also be taken into account. It will be observed that the number of patients admitted to the hospital has grown steadily, and it might therefore be supposed that part of the improvement in the case-fatality rate is due to the admission of less severe cases of the disease. This does not appear to be the case, and the main reason for the increase in admissions is that a larger proportion of patients are coming to the hospital from outside the Oxford region than ever before. Even so, in the most recent years the number of admissions has not increased. Secondly, it is essential to be certain that the improved results are indeed due to an advance in medical treatment and not to the use of emergency surgery.

It has now become exceptional for us to employ emergency colectomy in the treatment of an acute attack of ulcerative colitis. A few patients fail to respond to vigorous medical treatment or develop a complication, such as perforation of the colon, calling for surgical treatment, but they are a small proportion of the total. It is our experience that emergency colectomy should be avoided whenever possible in the treatment of an acute attack of ulcerative colitis and that the major use of surgery lies in elective operation for the patient who has troublesome chronic disease or who develops some complication which cannot be managed by medical means alone.

There are therefore excellent reasons for the conclusion that the improved results obtained in recent years represent an improvement in medical management. It would be wrong, of course, to attribute the improvement entirely to the use of local corticosteroid therapy, especially as this form of treatment is usually combined with systemic corticosteroid therapy. However, the principles of general medical care now employed have been in force in Oxford for at least a decade, while systemic corticosteroid therapy was introduced for this disease four years before the recent improvement in results. The exact coincidence of the improvement with the introduction of local corticosteroid therapy must be taken as strong presumptive evidence that this form of treatment has been a valuable addition to medical management.

Summary

Local corticosteroid treatment to the colon by means of a rectal drip of hydrocortisone hemisuccinate solution has been used in most in-patients with severe attacks of ulcerative colitis treated in Oxford since 1956. It appears to be best to combine it with systemic corticosteroid therapy. The simultaneous application of certain general medical measures is of profound importance.

Representative case-histories are given to illustrate some of the responses obtained and some of the problems entailed in the use of this form of treatment.

A provisional scheme for the medical treatment of a severe uncomplicated attack of ulcerative colitis, incorporating local corticosteroid therapy as one of its main features, has been drawn up. The essential features are as follows:

General medical measures should be instituted without delay and consist in (*a*) correction of dehydration and electrolyte depletion, special attention being paid to potassium depletion; (*b*) blood transfusion, to be repeated as often as necessary; (*c*) maintenance of nutritional state by high-calorie high-protein diet; and (*d*) vitamin supplements.

Systemic corticosteroid therapy should normally be applied by oral administration—for example, prednisolone in an initial dose of 15 mg. q.d.s. four times a day—but, if there is vomiting, treatment should begin with intravenous prednisolone phosphate, 25 mg. twice daily.

Local corticosteroid therapy consists in a rectal drip of 100 mg. of hydrocortisone hemisuccinate sodium in saline, morning and evening. Retention of the evening drip is facilitated by preliminary intravenous injection of propantheline bromide, but overdosage with this agent must be avoided.

Sulphonamides and antibiotics occupy a secondary role. Broad-spectrum antibiotics should not normally be given by mouth in ulcerative colitis, but they can be used parenterally for a few days at the start of treatment if there is high fever.

Since the addition of local corticosteroid therapy to the medical treatment of ulcerative colitis the case-fatality rate for in-patients admitted to two Oxford hospitals has shown a sharp decrease, and is now about

1.5%, after having been steadily around 8% during the previous 12 years. The evidence that at least a part of this recent improvement in results is directly due to local corticosteroid treatment is discussed.

I am grateful to Miss Betty Merry, of the Records Department, Radcliffe Infirmary, for assistance in preparing the Table and Chart, and to Dr. A. H. T. Robb-Smith, chairman of the Records Committee, for permission to use these data.

REFERENCES

Bargen, J. A. (1955). *Sth. med. J. (Bgham, Ala.)*, **48**, 192.
Lagercrantz, R. (1949). *Acta paediat. (Stockh.)*, Suppl. No. 75, p. 89.
—— (1955). Ibid., **44**, 302.
Morrison, L. M. (1952). *Gastroenterology*, **21**, 133.
—— (1953). *J. Amer. med. Ass.*, **151**, 366.
Spriggs, A. I., Smith, R. S., Griffith, H., and Truelove, S. C. (1958). *Lancet*, **1**, 1039.
Svartz, N. (1942). *Acta med. scand.*, **110**, 577.
—— (1948). Ibid., Suppl. No. 206, p. 465.
—— (1954). *Gastroenterology*, **26**, 26.
—— (1956). *Gastroenterologia (Basel)*, **86**, 683.
Truelove, S. C. (1956). *Brit. med. J.*, **2**, 1267.
—— (1957). Ibid., **1**, 1437.
—— (1958). Ibid., **2**, 1072.
—— (1960). Ibid., **1**, 464.
—— and Witts, L. J. (1954). Ibid., **2**, 375.
Watkinson, G. (1958). Ibid., **2**, 1078.

THE RESEMBLANCE BETWEEN SARCOIDOSIS WITH HYPERCALCAEMIA AND HYPERPARATHYROIDISM

BY

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Hypercalcaemia was first observed in sarcoidosis by Harrell and Fisher (1939); since then it has been recognized with increasing frequency, and probably occurs in at least 5% of cases (Longcope and Freiman, 1952). If left untreated it may lead to nephrocalcinosis, which is the commonest cause of renal failure in sarcoidosis (Citron, 1955). The metabolic abnormality in this condition closely resembles vitamin-D intoxication, with an increased absorption of calcium from the gut which is reversible by cortisone (Anderson *et al.*, 1954; Henneman *et al.*, 1956).

In this paper we report a case of sarcoidosis with hypercalcaemia in which there was an unusually close biochemical resemblance to hyperparathyroidism and discuss the differential diagnosis between the two conditions. This differentiation is important because excellent treatment is available for both; that it may also be difficult is shown by reports of at least 10 patients with sarcoidosis who have been subjected to operation because they were suspected of having a parathyroid adenoma (Albright and Reifenstein, 1948; Westra and Visser, 1949; Howard *et al.*, 1949; Klatskin and Gordon, 1953; Anderson *et al.*, 1954; Davidson *et al.*, 1954; Scholz and Keating, 1956; Hauch and Fisher, 1957).

Case Report

A married man aged 48 was referred to one of us (P. E.) for investigation of splenomegaly and admitted to St. Stephen's Hospital on September 3, 1956. He complained of tiredness and shortness of breath on exertion for one year and loss of appetite, loss of weight, constipation, lower abdominal pain, and increasing thirst and nocturnal frequency and polyuria for two months. At the age of 2 he had tuberculous cervical glands removed. In 1939 he first noticed pain and swelling in the ankles, and over a period of many years he developed slight outward bowing of the tibiae. He was given calciferol for three months for these symptoms in 1946, but he had not received vitamin D in any form after that time.

His wife had quiescent pulmonary tuberculosis. He had been an engineer for most of his life, but recently he had worked in the open air as a builder's labourer. His diet was adequate and had not recently altered, and he had never taken excessive amounts of milk or alkali.

On examination he had a ruddy complexion and did not look ill. There were numerous firm, moderately enlarged axillary, inguinal, and femoral lymph nodes, and the firm edges of both liver and spleen were palpable 2 in. (5 cm.) below the costal margins. The blood-pressure was 160/100, and the fundi were normal. There were bands of calcification in both corneae. The tibiae were bowed outwards and the knees separated by 1½ in. (3.8 cm.). The patient's weight was 130 lb. (59 kg.), height 63 in. (160 cm.) (crown to pubis 31½ in. (80 cm.), pubis to heels 31½ in.), and span 67 in. (170 cm.).

The urine contained a trace of protein and a few pus cells and granular casts; it was sterile, and culture for tubercle bacilli was negative. No Bence Jones protein was detected. The specific gravity range was 1006–1010. An intravenous pyelogram showed impaired concentration only. The haemoglobin was 10.5 g./100 ml. and E.S.R. 68 mm. in one hour (Westergren). Results of biochemical determinations on blood were: urea, 55 mg./100 ml.; calcium, 12.9 mg./100 ml.; inorganic phosphorus, 2.6 mg./100 ml.; alkaline phosphatase, 3.9 units (King–Armstrong); bilirubin, 0.5 mg./100 ml.; zinc sulphate turbidity, 16 units; albumin, 3.5 g./100 ml.; globulin 4.4 g./100 ml. Electrophoresis showed a slight increase in gamma-globulin. The Mantoux test was positive to 1/100. A skeletal survey was normal. *X*-ray examination of the chest showed increased striations in both lower zones. Biopsy of a right axillary gland showed histological appearances typical of sarcoidosis.

After four weeks in hospital with no treatment except bed rest the patient felt much better and had gained 4½ lb. (2 kg.) in weight; the serum calcium had fallen to 10.9 mg./100 ml. and the serum inorganic phosphorus to 2.2 mg./100 ml. However, the E.S.R. was still raised (67 mm. in one hour), the blood urea was 56 mg./100 ml., and maximum urine specific gravity 1012; a 24-hour specimen of urine contained 465 mg. of calcium in 960 ml. Because of the hypercalciuria and renal insufficiency he was started on cortisone 100 mg. daily despite the absence of symptoms and the normal serum calcium. The E.S.R. fell progressively, the haemoglobin increased to 13.5 g./100 ml., and he continued to gain weight. The serum calcium remained at the upper limit of normal (see Fig. 1).

After two weeks the 24-hour urine calcium was still 420 mg., and after one week on a low-calcium diet (less than 200 mg. daily) it was 326 mg. Despite the persistence of hypercalciuria there was a gradual improvement in renal function; after a month's treatment the maximum urine specific gravity had risen to 1018, the urine no longer contained any protein casts or pus cells, and there had been a gradual fall in blood urea. After three months' treatment the corneal calcification had almost disappeared. The dose of cortisone was reduced progressively to 37.5 mg. daily, but later had to be increased to 50 mg. daily. One year after treatment was started the 24-hour urine calcium excretion was 294 mg. and the patient was symptom-free; however, the serum calcium remained between 10.5 and 11.5 mg./100 ml. The affected lymph nodes gradually became smaller, but there was no significant change in the spleen or liver for two years. However, when the patient was last seen (October, 1959) his spleen was only just palpable.

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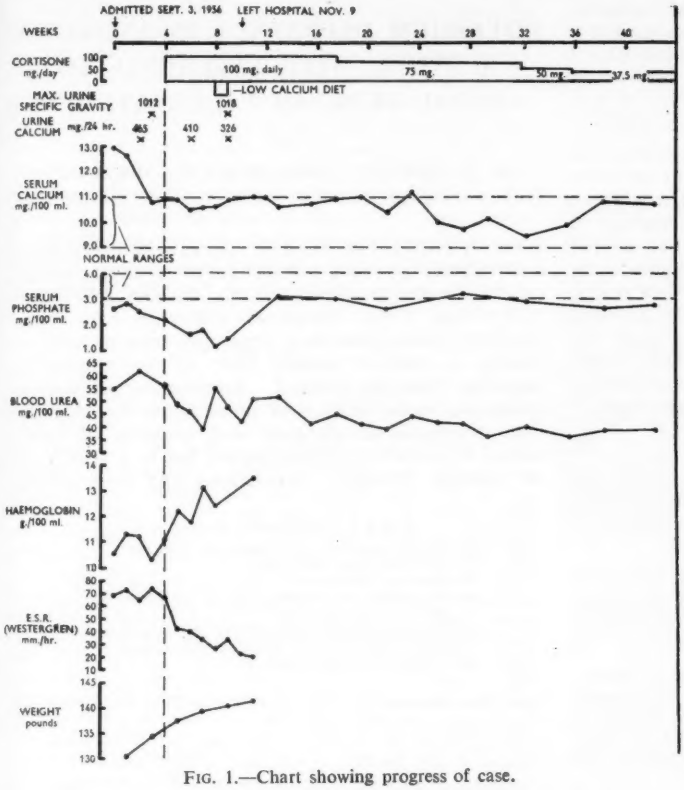

FIG. 1.—Chart showing progress of case.

	Serum P mg./100 ml.	Urine P mg./24 hr.	Urine P mg./min.	Clearance ml./min.
1. Before treatment ...	2·5	930	0·65	25·8
2. After cortisone 100 mg. daily × 14	1·6	460	0·32	20·0
3. After a low-calcium diet × 7	1·5	440	0·31	20·4
4. After treatment for 21 months	2·9	—	0·81	27·9

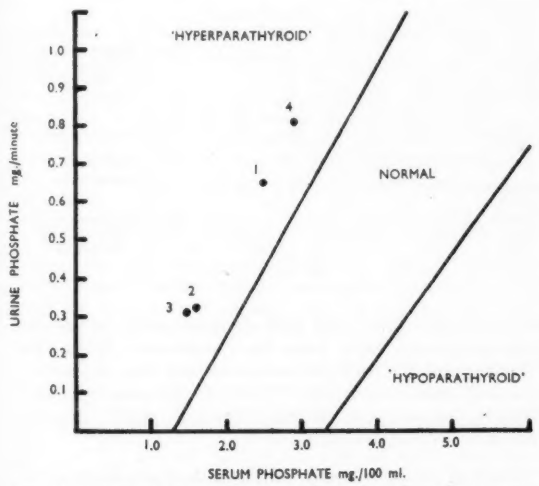

FIG. 2.—Rates of phosphate excretion plotted against serum level; with normal limits taken from Herbert, 1951.

Studies in Phosphate Excretion

The phosphate excretion data are tabulated (Fig. 2). On the first three occasions urine was collected for 24 hours and blood taken at 9.30 a.m. On the last occasion urine was collected for one hour with the patient fasting and blood was taken midway.

In Fig. 2 the rates of phosphate excretion are plotted against serum level, with the normal limits established by Herbert (1951). All the points fall in the "hyperparathyroid" range, indicating reduced tubular reabsorption.

Discussion

The usual biochemical criteria for the diagnosis of primary hyperparathyroidism are a high serum calcium, a low serum phosphate, and increased loss of calcium in the urine (Albright and Reifenstein, 1948). In addition, it is usually possible to demonstrate reduced tubular reabsorption of phosphate (Nordin and Fraser, 1956). All these criteria were fulfilled in our patient, and it is fortunate that the diagnosis of sarcoidosis was clearly established on other grounds.

In the differential diagnosis between the two conditions much stress has been laid on the level of serum phosphate, which is usually normal in sarcoidosis and low in hyperparathyroidism, in the absence of renal failure (Albright and Reifenstein, 1948). However, in at least five cases of sarcoidosis the serum phosphate has been below 3 mg./100 ml. before treatment (Longcope and Freiman, 1952; Klatskin and Gordon, 1953; Davidson *et al.*, 1954; Scholz and Keating, 1956), and a normal level is quite common in hyperparathyroidism (Chambers *et al.*, 1956).

Parathyroid hormone reduces the tubular reabsorption of phosphate (Jacobs and Verbanck, 1953), and this effect has been used as the basis of various diagnostic tests (Nordin and Fraser, 1956; Chambers *et al.*, 1956). However, if renal failure is present, tubular reabsorption of phosphate is progressively reduced (Goldman and Bassett, 1954), and, under these circumstances, tests of phosphate excretion are of little diagnostic help (Dent, 1956). Furthermore, reduced phosphate reabsorption is also found in other diseases associated with hypercalcaemia, including sarcoidosis (Chambers *et al.*, 1956), malignant disease (Schatten *et al.*, 1959), and myelomatosis (Thomas *et al.*, 1958). In the present case it was tempting to link the impaired phosphate reabsorption with the short stature (height 4 in. (10 cm.) less than span) and the development of pain and slight deformity of the legs, and to postulate that the patient had in a mild form the defect characteristic of resistant rickets.

The most reliable means of distinguishing the two conditions is by observing the effect of cortisone, which regularly corrects the hypercalcaemia of sarcoidosis, but has no significant effect on the hypercalcaemia of hyperparathyroidism (Dent, 1956). Neither result is specific, since cortisone may correct the hypercalcaemia in some, but not all, cases of myelomatosis (Thomas *et al.*, 1958), Hodgkin's disease (Kabakow *et al.*, 1957), and metastatic

malignancy (Myers, 1958). However, a fall in serum calcium with cortisone is very good evidence against a diagnosis of hyperparathyroidism. Correspondingly, if a raised serum calcium does not fall with cortisone it should not be attributed to sarcoidosis even if that disease is known to be present (Snapper *et al.*, 1958).

In our patient the initial change in serum calcium on bed rest alone precluded the diagnostic use of cortisone but was of great diagnostic value in itself. The patient's symptoms of anorexia, loss of weight, and constipation, which were probably due to hypercalcaemia, started while he was working in the open air, exposed to the sun. The fall in serum calcium, which was accompanied by symptomatic improvement, occurred after removal from this exposure. This relationship to sunlight has been observed before (Mather, 1957), and Dent (1958) has shown that ultra-violet irradiation may exacerbate both hypercalcaemia and hypercalciuria in sarcoidosis.

Summary

The case is presented of a patient with sarcoidosis and hypercalcaemia in whom decreased tubular reabsorption of phosphate was demonstrated, producing a biochemical resemblance to primary hyperparathyroidism.

The differential diagnosis between the two conditions is discussed, and it is concluded that tests of phosphate excretion may be misleading, but that the response to cortisone gives valuable information.

We thank Dr. A. D. Everett for referring the patient to us, Dr. A. Gordon Signy for his help with the histological and biochemical investigations, Dr. F. Harwood Stevenson for his criticism of the manuscript, and Professor C. E. Dent for his continued help and advice in the management of the patient.

REFERENCES

Albright, F., and Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease*. Williams and Wilkins, Baltimore.

Anderson, J., Harper, C., Dent, C. E., and Philpot, G. R. (1954). *Lancet*, **2**, 720.

Chambers, E. L., Gordan, G. S., Goldman, L., and Reifenstein, E. L. (1956). *J. clin. Endocr.*, **16**, 1507.

Citron, K. M. (1955). *Postgrad. med. J.*, **31**, 516.

Davidson, C. N., Dennis, J. M., McNinch, E. R., Willson, J. K. V., and Brown, W. H. (1954). *Radiology*, **62**, 203.

Dent, C. E. (1956). *Brit. med. J.*, **1**, 230.

—— (1958). *Proc. VIII Middle East Medical Assembly*, p. 162.

Goldman, R., and Bassett, S. H. (1954). *J. clin. Invest.*, **33**, 1623.

Harrell, G. T., and Fisher, S. (1939). Ibid., **18**, 687.

Hauch, E. W., and Fisher, R. L. (1957). *Calif. Med.*, **86**, 333.

Henneman, P. H., Dempsey, E. F., Carroll, E. L., and Albright, F. (1956). *J. clin. Invest.*, **35**, 1229.

Herbert, F. K. (1951). In *Recent Advances in Clinical Pathology*, 2nd ed., edited by S. C. Dyke. Churchill, London.

Howard, J. E., Carey, R. A., Rubin, P. S., and Levine, M. D. (1949). *Trans. Ass. Amer. Phycns.*, **62**, 264.

Jacobs, E., and Verbanck, M. (1953). *Acta med. scand.*, **145**, 143.

Kabakow, B., Mines, M. F., and King, F. H. (1957). *New Engl. J. Med.*, **256**, 59.

Klatskin, G., and Gordon, M. (1953). *Amer. J. Med.*, **15**, 484.

Longcope, W. T., and Freiman, D. G. (1952). *Medicine (Baltimore)*, **31**, 1.

Mather, G. (1957). *Brit. med. J.*, **1**, 248.

Myers, W. P. L. (1958). *Cancer*, **11**, 83.

Nordin, B. E. C., and Fraser, R. (1956). In *Ciba Foundation Symposium on Bone Structure and Metabolism*, p. 222. Churchill, London.

Schatten, W. E., Ship, A. G., Pieper, W. J., and Bartter, F. C. (1958). *Ann. Surg.*, **148**, 890.

Scholz, D. A., and Keating, F. R. (1956). *Amer. J. Med.*, **21**, 75.

Snapper, I., Yarvis, J. J., Freund, H. R., and Goldberg, A. F. (1958). *Metabolism*, **7**, 671.

Thomas, W. C., Connor, T. B., and Morgan, H. G. (1958). *J. Lab. clin. Med.*, **52**, 11.

Westra, S. A., and Visser, J. F. (1949). *Ned. T. Geneesk.*, **93**, 18.

POTASSIUM DEFICIENCY IN ANOREXIA NERVOSA, WITH REFERENCE TO RENAL TUBULAR VACUOLATION*

BY

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Electrolyte deficiency in anorexia nervosa may create a therapeutic problem, not mentioned in several recent papers, in the treatment of this disorder (Williams, 1958; Wall, 1959). Diagnostic difficulties may arise, especially when secondary renal involvement occurs, leading to serious consideration of the alternative diagnoses listed in Table I. Investigation of a case presenting typical features of anorexia nervosa together with hypokalaemic alkalosis, and evidence of renal failure with chronic pyelonephritis, led to a search of the relevant literature. Sunderman and Rose (1948) described the first case with hypokalaemic alkalosis. Seventeen cases have now been reported (Table II). Elkinton and Huth (1959) have reviewed the electrolyte disorders that may occur. Most of the cases showed alkalosis, some hyponatraemia, and eight showed evidence of renal dysfunction.

TABLE I.—*Differential Diagnosis*

1. Hypopituitarism and Addison's disease
2. Malabsorption syndrome
3. Habitual purgation
4. Potassium- and sodium-losing nephritis
5. Primary aldosteronism
6. Chronic nephritis and chronic pyelonephritis
7. Pineal tumours and hypothalamic lesions
8. Familial periodic paralysis

TABLE II.—*Summary of Cases Reported to Date (Serum Levels in mEq/l.)*

Authors		Age	Na	K	Cl	HCO_3	Evidence of Renal Involvement	Notes
Sunderman and Rose (1948)		26	—	3·0	58	62	—	Enemas and vomiting
Elkinton *et al.* (1951)			127	2·8	74	44·5	Yes	No vomiting; laxatives
Beck and Brochner-Mortensen (1954; Case 26)		28	137	2·6	96	—	,,	Vomiting. Blood urea 51 mg.; 26 mg. after treatment
Luft and Sjögren (1954)	1	26	139	2·2	45	49	,,	Vomiting and tetany. Albuminuria
	2	34	139	1·5	98	21	,,	No vomiting. No albuminuria
Klotz and Lumbroso (1955)		29	141	2·0	—	55	—	Vomiting
Rossier *et al.* (1955)	St.H.	28	140	2·0	74	45	—	—
	F.E.	24	—	2·9	—	29	Yes	Pyelonephritis
	K.M.	24	146	2·6	97·4	28	—	Diarrhoea and vomiting
	M.M.	23	142	3·1	78	37	—	Vomiting
	T.E.	17	148	3·6	105	29	—	—
	H.A.	28	143	3·4	—	24	—	—
Siebenmann (1955)		27	133	1·8	109	20	Yes	Took laxatives
Forssman (1955)		17	143	3·0	50	—	,,	Said to have nephritis
Ljunggren *et al.* (1957)			128	2·9	85	40	—	—
Elkinton and Huth (1959)	A.B.	29	120	1·7	53	52	Yes	Magnesia
	M.B.	43	126	2·4	69	44	—	Vomiting and magnesia

*Based on a paper read at a meeting of the Royal Australasian College of Physicians at Auckland on September 17, 1959.

It is now generally accepted that potassium depletion can cause renal dysfunction, resulting in thirst, polyuria, isosthenuria with tubular vacuolation, and often pyelonephritic changes (Relman and Schwartz, 1958; Milne *et al.*, 1957). The case of anorexia nervosa described by Siebenmann (1955) is of particular interest in that post-mortem examination showed vacuolation of the renal tubules and fragmentation of heart muscle. Diarrhoea from aperients must have contributed to the severe potassium depletion in this case. Three cases of anorexia nervosa in which there was no history of habitual purgation are reported. One of these showed tubular vacuolation in a renal biopsy and at necropsy.

Case 1

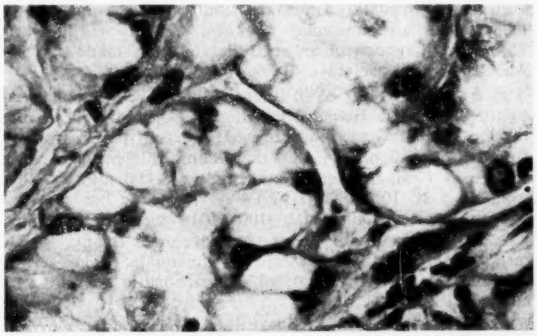
The patient was a married woman aged 38. She was admitted to the Palmerston North Hospital in July, 1957, with loss of weight, amenorrhoea, and sensitivity to cold for one year and lack of energy for six months. Her appetite was variable. Usually she claimed that it was good, but her husband said that she ate very little at the onset of illness and vomited frequently. It appears that what she regarded as a good appetite was small by ordinary standards. Her skin was dry, with a yellowish tinge, and a growth of fine downy hair was noticeable on the face. Blood-pressure was 108/70. She had a normochromic anaemia (haemoglobin 9.5 g./100 ml.). The serum cholesterol was 480 mg./100 ml.; and potassium 3.2, sodium 135, chloride 108, and bicarbonate 25 mEq/l. The urine contained albumin with numerous granular casts. The specific-gravity range was 1009–1026. *Escherichia coli* was cultured from the urine. 25% of a 1,500-ml. water load was excreted before and 90% after 50 mg. of cortisone. Urine 17-ketosteroids excretion was 4.5 mg./day and 17-ketogenic steroids 3.8 mg./day. An oral glucose-tolerance curve rose from a fasting level of 85 to 100 mg./100 ml. at three-quarters of an hour, falling to 50 mg. at one and a half hours. B.M.R. +1%. No excess of fat globules was found in the faeces. Barium-meal examination and follow-through showed nothing abnormal.

The psychiatric findings (Dr. S. Mirams) were consistent with a diagnosis of anorexia nervosa. The patient was said to have changed mentally after having a stillborn child, 11 years before. A tubal ligation followed this. Her husband fell below her in standards of social behaviour and intelligence, and was an alcoholic. The home was unhappy and she was frigid.

Arrangements were made for fat- and electrolyte-balance studies, but the patient could not be persuaded to re-enter hospital. A trial of prednisone, 15 mg. daily, as an out-patient produced an improvement in appetite and she gained 7 lb. (3.2 kg.) in weight, but the serum potassium remained low (3.7 mEq/l.) and it was thought inadvisable to continue. In February, 1958, her weight fell to 5 st. 8 lb. (35.4 kg.), with weakness, marked anorexia, and hypotension (90/60). The serum potassium was 2.3 mEq/l. She again refused admission.

In June, 1958, she agreed to out-patient treatment. The serum potassium was lower at 2.2 mEq/l., total N.P.N. 59 mg./100 ml., and cholesterol 320 mg./100 ml. A renal biopsy showed marked tubular vacuolation indistinguishable from the post-mortem changes (see Fig.). Oral potassium chloride was prescribed, but it is very doubtful if she took much if it, as she was admitted eight days later with pneumonia and hypokalaemic paralysis which failed to respond to an intravenous infusion of potassium chloride and antibiotics. She died six hours later. The serum potassium, chloride, and sodium before treatment were 1.3, 103, and 135 mEq/l. respectively and the urine potassium 9.0, chloride 58, and sodium 61 mEq/l. (normal potassium level greater than 10 mEq/l.: Schwartz, 1955).

Post-mortem Examination (Dr. W. L. Kenealy).—The right kidney weighed 120 g. and the left 110 g. They were pale, with no reduction of cortical tissue. There was a small subcapsular haematoma at the biopsy site. Sections of the kidney confirmed the biopsy finding of marked vacuolation of the cells lining the proximal convoluted tubules and a minor degree of chronic pyelonephritis (see Fig.). The pituitary and endocrine glands were normal. A penicillin-resistant *Staphylococcus aureus* was cultured from the bronchi, which were inflamed, and from the left lower lobe, which was consolidated.



Case 1. Photomicrograph showing vacuolation of cells lining the proximal convoluted tubules. (×264.)

Comment.—The patient was thought to be a case of anorexia nervosa with prolonged potassium deficiency resulting in tubular vacuolation and minor chronic pyelonephritic changes.

Case 2

The patient, a married woman aged 30, was admitted to the Green Lane Hospital, Auckland, in March, 1956, with intermittent paralysis of the legs. Swelling of the ankles, thirst, and nocturia had been present for about one year. Six years earlier, when her eldest child was born, her periods ceased. They had been irregular before this and she had been given injections in the hope of restoring a normal rhythm. It was about this time that family difficulties arose and she separated from her husband. There was no history of taking purgatives.

She weighed only 4 st. (25.4 kg.). Breast development was poor. There was fine downy hair all over the body, but hair distribution was otherwise normal. The skin was dry. Her blood-pressure was 100/84 and there was a generalized loss of muscle power. The serum potassium was 1.85, chloride 107, sodium 154, and bicarbonate 29 mEq/l. The total N.P.N. was 28 mg./100 ml., haemoglobin 11.3 g./100 ml., and serum cholesterol 190 mg./100 ml. Coliform bacilli were cultured from the urine, which contained large numbers of white cells. The urine potassium varied between 1 and 3 mEq/l., 17-ketosteroids 4.5 mg./day, and F.S.H. less than 48 units per day. Cardiography showed typical hypokalaemic changes. She refused medical advice for several years.

In 1958 her weight fell as low as 3 st. 7 lb. (22.2 kg.). In March, 1959, she was admitted to the Auckland Hospital with piles and a fistula-in-ano. She weighed 4 st. 2 lb. (26.3 kg.) at this time. A catheter urine specimen contained no casts, cells, or organisms. The serum albumin was 2.5 and globulin 3.6 g./100 ml. In September, 1959, her doctor reported that with his assistance she had improved considerably and was again living with her husband.

Comment.—An otherwise typical case of anorexia nervosa with hypokalaemic paralysis.

Case 3

A spinster aged 33 came under the care of Dr. C. P. Powles, of Wanganui, in 1952, with depression and anorexia, insomnia, loss of weight, and nausea. She had an obsessional personality and there were emotional problems concerning her home life and her work. She developed amenorrhoea in 1953 and has had infrequent scanty periods since. She complained of thirst and admitted to occasional vomiting. Cachexia was marked, and there was some growth of fine hair and muscular weakness. Blood-pressure was 95/70. A diagnosis of anorexia nervosa was made and she was treated accordingly.

Her symptoms varied in intensity until she was admitted to the Wanganui Hospital in March, 1956, with increasing tiredness, nausea, and vomiting. Her serum potassium was found to be 3.3 mEq/l. and the sodium 135 mEq/l. In a relapse in 1958, the serum potassium was 3.0 mEq/l. She weighed 5 st. 10 lb. (36.3 kg.). At this time her specific-gravity range was limited to 1008–1016 and urea clearance was 59% of normal. Later she developed tetany, which responded to intravenous calcium gluconate. The serum calcium was 5–6 mg./100 ml.; bicarbonate was 26 and chloride 99 mEq/l.

In September, 1958, she was reinvestigated in Dunedin. At this time she weighed only 5 st. (31.8 kg.) and her serum potassium was 3.5 mEq/l., sodium 139, chloride 108, but the urinary potassium was low at 7 mEq/l. The total N.P.N. was 28 mg./100 ml., the urine concentration 1030, and the urea concentration 3.5%.

TABLE III.—*Lowest Figures Recorded in mEq/l. Urine Levels in Parentheses. All Female Cases*

Case	Weight	Age	N.P.N./ 100 ml.	Na	K	Cl	HCO_3	Notes
1	5 st. 8 lb. (35·8 kg.)	38	86	135 (61)	1·3 (9·0)	103 (58)	22	Paralysis. Renal lesion
2	4 st. (25·4 kg.)	30	28	154	1·85 (1·0)	107	29	Paralysis. Urinary infection
3	5 st. (31·75 kg.)	33	28mg.	139	3·5, 3·0 (7·0)	108	N.	Transient renal involvement

Comment.—A long-standing case of anorexia nervosa with potassium depletion which was probably responsible for the thirst and transient impairment of renal function.

Discussion

Squires and Huth (1959), in an experimental potassium depletion in man, have shown that a negative balance occurs if intake is reduced from 14 to 1 mEq/day. Presumably the potassium depletion of anorexia nervosa is produced in the same way. Elkinton and Huth (1959), in a comprehensive review of this problem, emphasize that it is very difficult to be sure that these patients are not vomiting or taking purgatives. Either of these factors might aggravate the potassium deficiency. Though steatorrhoea was not seriously considered in the present cases it was not entirely excluded as a possible cause of potassium loss. These patients are rarely co-operative enough to conduct reliable fat-balance tests, and it is to be hoped that faecal potassium estimation, labelled fat- (Rowlands, 1959) and D-xylose (Butterworth *et al.*, 1959) absorption tests, and jejunal biopsy (Shiner, 1959) will enable more complete investigation of small-bowel function if further cases are encountered. Ljunggren *et al.* (1957) demonstrated low intracellular potassium levels in two of three cases of anorexia nervosa with serum levels below 3.7 mEq/l., indicating that the low serum and urine levels do reflect an intracellular potassium depletion. The low serum-chloride levels found can be partly explained by the extracellular alkalosis which occurs in experimental potassium depletion when sodium is not withheld (Fourman, 1954; Huth *et al.*, 1959). Conversely, the three cases without alkalosis may have been in salt depletion, though the serum sodium was depressed in only two of these. Chloride loss from vomiting may have aggravated the alkalosis to the point where the urine became alkaline, so that paradoxical aciduria did not always occur.

The possibility that hypersecretion of the adrenal cortex could explain the hypokalaemic alkalosis is discounted, as adrenal dysfunction has not been demonstrated in anorexia nervosa (Bliss and Migeon, 1957). The urine 17-ketosteroids were low in two of the present cases. Primary aldosteronism is excluded by the low urine levels of potassium. The increased water excretion in Case 1 after cortisone is difficult to explain.

Kleeman and Maxwell (1959) have cast some doubt on whether the thirst of potassium depletion is entirely of renal origin and offer evidence of a direct effect on the hypothalamus or posterior pituitary. Histochemical studies of the vacuolar lesion suggest that the translucencies are due to swelling of mitochondria (Pearce and MacPherson, 1958). This lesion is reversible so far as is known, but the associated pyelonephritic changes may be permanent (Relman and Schwartz, 1958). *E. coli* infection is a frequent complication, and Woods *et al.* (1959) have shown that potassium deficiency predisposes to experimental infection with this organism, but the possibility remains that prolonged deficiency may result in irreversible changes resembling those of pyelonephritis (Stanbury, 1958). Albuminuria, pyelonephritis, or nephritis was mentioned in 8 of the 17 cases in the literature (Table II), so it seems probable that tubular vacuolation was present in some of them.

The complex clinical picture produced by electrolyte and renal changes in anorexia nervosa may well have led to misdiagnosis in the past, accounting for the paucity of information available on this subject.

Summary and Conclusions

Seventeen reported cases of anorexia nervosa with hypokalaemia are summarized. Eight showed some evidence of renal disorder. Habitual purgation complicated the only case shown to have the tubular lesion of potassium depletion.

Three further cases with hypokalaemia are described, one showing tubular vacuolation.

It is thought that the potassium depletion is due to a deficient intake, aggravated in some cases by vomiting, and in some by purgation. Malabsorption may be more certainly excluded if further cases become available.

Fatal paralysis and possibly irreversible renal changes may occur if this complication is not recognized. Five of the 20 patients had died at the time of reporting.

Conventional treatment should correct the deficit, but oral or intravenous potassium chloride may prove necessary.

I am indebted to Dr. D. S. Dickson for providing details of Case 2; to Dr. C. P. Powles for allowing me to see

Case 3; to Dr. R. W. Medlicott and Professor J. E. Caughey for lending their records of Case 3; to Miss Anne Simmonds for the biochemical estimations in Case 1; and to Mr. Hamblyn for the photomicrograph. Dr. W. L. Kenealy and Dr. T. H. Pullar have given invaluable assistance in the preparation of this paper.

REFERENCES

Beck, J. C., and Brochner-Mortensen, K. (1954). *Acta med. Scand.*, **149**, 409.
Bliss, E. L., and Migeon, C. J. (1957). *J. clin. Endocr.*, **17**, 766.
Butterworth, C. E., Perez-Santiago, E., de Jesus, J. M., and Santini, R. (1959). *New Engl. J. Med.*, **261**, 157.
Elkinton, J. R., and Huth, E. J. (1959). *Metabolism*, **8**, 376.
—— Squires, R. D., and Crosley, A. P. (1951). *J. clin. Invest.*, **30**, 369.
Forssman, B. (1955). *Nord. med.*, **54**, 1373.
Fourman, P. (1954). *Clin. Sci.*, **13**, 93.
Huth, E. J., Squires, R. D., and Elkinton, J. R. (1959). *J. clin. Invest.*, **38**, 1149.
Kleeman, C. R., and Maxwell, M. H. (1959). *New Engl. J. Med.*, **260**, 268.
Klotz, H. P., and Lumbroso, P. (1955). *Sem. Hôp. Paris*, **31**, 440.
Ljunggren, H., Ikkos, D., and Luft, R. (1957). *Acta endocr. (Kbh.)*, **25**, 209.
Luft, R., and Sjögren, B. (1954). Ibid., **17**, 264.
Milne, M. D., Muehrcke, R. C., and Heard, B. F. (1957). *Brit. med. Bull.*, **13**, 15.
Pearce, A. G. E., and MacPherson, C. R. (1958). *J. Path. Bact.*, **75**, 69.
Relman, A. S., and Schwartz, W. B. (1958). *Amer. J. Med.*, **24**, 764.
Rossier, P. H., Staehelin, D., Bühlmann, A., Labhart, A. (1955). *Schweiz. med. Wschr.*, **85**, 465.
Rowlands, E. N. (1959). *Proc. roy. Soc. Med.*, **52**, 1.
Schwartz, W. B. (1955). *New Engl. J. Med.*, **253**, 601.
Shiner, M. (1959). *Proc. roy. Soc. Med.*, **52**, 10.
Siebenmann, R. E. (1955). *Schweiz. med. Wschr.*, **85**, 468.
Squires, R. D., and Huth, E. J. (1959). *J. clin. Invest.*, **38**, 1134.
Stanbury, S. W. (1958). *Advanc. intern. Med.*, **9**, 271.
Sunderman, F. W., and Rose, E. (1948). *J. clin. Endocr.*, **8**, 209.
Wall, J. H. (1959). *Amer. J. Psychiat.*, **115**, 997.
Williams, E. (1958). *Brit. med. J.*, **2**, 190.
Woods, J. W., Welt, L. G., Hollander, W., and Newton, M. (1959). *J. clin. Invest.*, **38**, 1056.

DIAGNOSIS AND TREATMENT OF TRICHOMONAL URETHRITIS IN MEN

BY

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Trichomonas vaginalis was first reported to be present in the genital tracts of male patients by Marchand in 1894. Since then many other instances and series of cases have been published. However, until recently the recorded incidence of infection in men has been low. With improved techniques and increasing interest in non-gonococcal urethritis during recent years, results have indicated that infestation with the parasite is more common than had formerly been supposed. There seems little doubt that the organism is one of the causes of genital infection in the male, though its precise importance in the aetiology of non-gonococcal urethritis is not yet determined.

The results of investigation have varied greatly in different hands. For example, Ackermann (1935) failed to find *T. vaginalis* in the urethral secretions of 37 men with non-gonococcal urethritis, though the parasite was present in the vaginal secretions of six of their consorts. Allison (1943) found *T. vaginalis* in 15% of a group of white patients with gonorrhoea or other genital infections and also in 200 negroes who had been rejected for military service because of venereal disease: 95% of the negro patients had urethral strictures. Feo (1944) found the parasite in 121 of 735 male negroes (16.4%), and in 23 of 191 male white patients (12%). Whittington (1957) found *T. vaginalis* in 15.3% of 326 men with non-specific urethritis. The highest recorded incidence is that of Coutts *et al.* (1955), who claimed that 68% of 2,482 male patients in Chile were infected with the parasite.

The object of this investigation was to examine in detail the clinical and bacteriological findings in a large series of male patients with trichomonal urethritis and to attempt to evaluate various forms of therapy.

Material and Methods

All the patients included in this series attended the Whitechapel Clinic of the London Hospital during the three years from January, 1956, to January, 1959. A detailed history was obtained from each patient and a thorough physical examination performed. Urethral specimens for microscopical examination were taken by the method advocated by Lanceley (1954) by gently stroking the urethral wall with a platinum loop. The slides were examined at once by dark-ground microscopy. In addition, smears of the urethral secretions were also stained with Gram's stain and examined microscopically under the 1/12-in. objective. Cultures for *T. vaginalis*, using the liquid liver medium of Feinberg and Whittington (1957), were performed in half of the cases. Stuart's transport medium was also inoculated with specimens from the urethra, and these were later transferred to MacLeod's chocolate agar. In a small number of cases the centrifuged deposit of urine was examined microscopically and cultures were performed. In all cases in which the organism was found attempts were made to persuade the consorts to attend for examination and, if necessary, treatment.

Diagnosis

T. vaginalis was found in 126 cases. During the same three-year period there were 2,300 infections described as non-gonococcal urethritis recorded at the clinic. Trichomonal urethritis, therefore, comprised 5.5% of the total infections diagnosed as non-gonococcal urethritis.

The average age of the patients was 33 years. There were 82 white patients and 44 of negro race.

Eighteen patients (14.3%) had no symptoms referable to the genito-urinary tract. Ninety patients (71.4%) complained of urethral discharge: the type of discharge was very variable, but in most cases was small in quantity, mucopurulent, and most obvious early in the morning before the first micturition; in a small proportion of cases, however, it was frankly purulent, and thick, and was present throughout the day. Itching inside the penis was complained of by 26 patients (20.6%), dysuria occurred in 15 (11.9%), frequency of micturition in 4 (3.2%), two had noticed blood-stained urethral discharge, and one complained of haematuria. Pain and swelling of an epididymis was the presenting manifestation in one case.

At the first examination 80 of the patients (63.5%) were found to have a urethral discharge. In the cases

of 38 patients (30.1%) no urethral discharge was seen at the first examination and urethral secretion was found only when the patients attended for early morning tests before passing the first morning urine. No evidence of discharge was found, even on early morning testing, in eight cases (6.3%).

T. vaginalis was found in the urethral scrapings in 112 of the 126 cases (88.8%). Cultures were performed in 63 cases and were positive in 58 (92%). In two cases the parasite was found in the centrifuged deposit of urine after scrapes and cultures had proved negative.

Gonococci were isolated from the urethral secretions of eight patients. In most of the remainder, the Gram-stained smear from the urethra showed between 10 and 20 pus cells per 1/12-in. microscopical field, a few epithelial cells, and a variety of Gram-positive and Gram-negative organisms. Cultures of the urethral discharge grew mainly streptococci, staphylococci, diphtheroids, and occasionally *Escherichia coli*.

Urethral stricture was found in 10 patients (7.9%), and all 10 showed a marked tendency to relapse after treatment, but the results of therapy improved after dilatation of the strictures.

The sexual partners of 67 of the patients were traced and attended for examination. *T. vaginalis* was demonstrated in the vaginal secretions of 57 (85%) of them. In several cases in the male the results of treatment were unsatisfactory until the consorts had been examined and treated.

Treatment

Little has been written about the treatment of trichomonal urethritis in the male. Liston and Lees (1940) believed that an alkaline urine inhibited the development of trichomonads and relieved symptoms. Strain (1945) favoured calcium mandelate by mouth. Harkness (1950) recommended urethro-vesical irrigations combined with prostato-vesicular massage, especially in cases with involvement of the prostate or seminal vesicles. Disappointing results were obtained with the systemic drug 2-acetylamino-5-nitrothiazole and with the antibiotic " trichomycin " (Catterall and Nicol, 1957), and so far a suitable oral therapy is not yet available.

It has been suggested that the disease is self-limiting in men and tends to spontaneous cure. In this regard, Lanceley and McEntegart (1953) observed three experimentally infected men and found the organism in the genital tract for from 4 to 94 days. The observations of Whittington (1957) on a group of 19 patients with trichomonal urethritis from whom treatment was withheld did not support the view that spontaneous recovery was a common happening. In this series no treatment was given to 14 patients with trichomonal urethritis. Two patients defaulted during follow-up, but the remaining 12 were observed for three months. Trichomonads were found in the urethral secretions or in the centrifuged deposit of urine in 10 of the patients throughout the period of follow-up. In the remaining two the parasite could not be found, though one of them continued to have mild symptoms. Thus the evidence, so far as it goes, indicates that spontaneous cure is probably exceptional.

A small group of 12 patients was treated with oxytetracycline, 250 mg. six-hourly for five days. In two cases the parasite disappeared from the urethral secretions during treatment and was not found again during the three-month follow-up period. In the other 10 cases trichomonads were present in the urethral secretions throughout the period of treatment and at the end of treatment.

The remaining 100 patients were all treated with urethro-vesical irrigations, using a variety of therapeutic agents. Fifty were each given 10 daily urethro-vesical irrigations, using a 1 in 8,000 solution of potassium permanganate. There were eight defaulters, leaving 42 patients for assessment. Twenty-five (59%) were regarded as cured in that no relapse occurred during the three-month follow-up period.

Thirty patients were treated with daily urethro-vesical irrigations for 10 days, using a 1 in 8,000 solution of oxycyanide of mercury. Four patients defaulted, leaving 26 for assessment. Of these 26 patients, 18 (69.2%) were regarded as cured after a follow-up period of three months.

Lastly, 20 patients were treated with 10 daily urethro-vesical irrigations, using a 1 in 10,000 solution of dequalinium chloride (" dequadin "). There was one defaulter in this group. Of the remaining 19 patients, 14 (73.6%) were regarded as cured after a follow-up period of three months.

The lowest cure rate in this series of patients treated with irrigations was almost 60%, which is higher than might be expected with the best form of treatment in female patients, and it is possible that the difficulties in detecting the organism in the male give an erroneously high cure rate and produce a false impression of the success of treatment.

Discussion

There is general agreement that symptoms may be mild or altogether absent in trichomonal infestations of the male urethra. In the present series the commonest complaint was of urethral discharge, and many patients complained of itching inside the penis. More serious symptoms, such as dysuria, frequency, haemorrhagic discharge, haematuria, and pain and swelling of an epididymis, did occur in a small number of patients.

The value of using both wet smears of the urethral scrapings and cultures in the diagnosis of trichomoniasis has been pointed out by Whittington (1957) and Nicol (1958). The use of the two methods in the follow-up also provides more rigid criteria for the cure of the condition. In 30% of the patients no evidence of urethritis or of urethral disease was detected when the patients were first examined during the day. The diagnosis in all these cases was made by examining the patient first thing in the morning before he had passed the morning urine. This early morning smear and culture test is of inestimable value in the investigation of cases of urethritis from whatever cause.

The most satisfactory method of treating trichomonal urethritis in men at the present time appears to be with urethro-vesical irrigations, using weak solutions of potassium permanganate, oxycyanide of mercury, or dequalinium chloride. If the consort is also treated and sexual intercourse stopped until the parasite is eradicated from the genital tract, a reasonably high cure rate may be expected. If relapse occurs, without the likelihood of reinfection, the possibility of urethral stricture should be considered and urethroscopy performed. It is, however, probable that more satisfactory treatment of this condition must await the discovery of a systemic trichomonicidal substance which is effective when given by mouth or by injection.

Summary and Conclusions

The symptoms and signs of 126 cases of trichomonal urethritis in male patients are reviewed. The use of fresh urethral scrapings and of urethral cultures are recommended for diagnosis and for follow-up. The value of the early morning smear and culture test in diagnosis is stressed.

The results of treatment in 112 cases are described. Moderately satisfactory results can be obtained by urethro-vesical irrigations, using a weak solution of potassium permanganate, oxycyanide of mercury, or dequalinium chloride.

The presence of urethral stricture may be responsible for some cases of failure of treatment and of early relapse.

I thank Mr. Ambrose King for permission to publish these findings and for his constant help and encouragement. This work was carried out under the aegis of the Medical Research Council Working Party on Non-Specific Urethritis, with the aid of a grant from the U.S. Department of Public Health.

REFERENCES

Ackermann, A. (1935). *Derm. Z.*, **71**, 132.
Allison, G. G. (1943). *Sth. med. J. (Bgham, Ala.)*, **36**, 821.
Catterall, R. D., and Nicol, C. S. (1957). *Brit. med. J.*, **2**, 29.
Coutts, W. E., Vargas-Salazar, R., Silva-Inzunza, E., Olmedo, R., Turteltaub, R., and Saavedra, J. (1955). Ibid., **2**, 885.
Feinberg, J. G., and Whittington, M. J. (1957). *J. clin. Path.*, **10**, 327.
Feo, L. G. (1944). *Amer. J. trop. Med.*, **24**, 195.
Harkness, A. H. (1950). *Non-Gonococcal Urethritis*, p. 228. Livingstone, Edinburgh.
Lanceley, F. (1954). *Brit. J. vener. Dis.*, **30**, 163.
—— and McEntegart, M. G. (1953). *Lancet*, **1**, 668.
Liston, W. G., and Lees, R. (1940). *Brit. J. vener. Dis.*, **16**, 34.
Marchand, F. (1894). *Zbl. Bakt.*, **15**, 709.
Nicol, C. S. (1958). *Brit. J. vener. Dis.*, **34**, 192.
Strain, R. E. (1945). *J. Urol. (Baltimore)*, **54**, 483.
Whittington, M. J. (1957). *Brit. J. vener. Dis.*, **33**, 80.

TRACTION ALOPECIA

BY

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Baldness is causing an increasing number of women to attend the skin clinic of Khartoum Civil Hospital. Many cases present the characteristic features of alopecia areata. In others there is evidence of infection or endocrine disturbance. In 12 patients, however, the diagnosis was not obvious. The alopecia seemed to result directly from the traditional hair style of the Northern Sudanese women.

The Northern Sudan Coiffure

The women of the Northern Sudan are extremely conservative in their cosmetic habits and retain the same hair style throughout life. The customary coiffure consists of many tight plaits, sometimes numbering 120 or more, which hang from the middle of the scalp. A coronal parting is introduced to divide the hair into four quadrants (Fig. 1). The natural length of the hair is often augmented by braiding black silk thread into the plaits. This gives the hair a greater apparent length

FIG. 1.—Scalp of Northern Sudanese woman showing characteristic hair style and alopecia.

(Fig. 2), the tresses often reaching to the buttocks. The silk incorporated in the plaits may weigh as much as 16 oz. (450 g.). The hair is braided every one to three months, the process of unplaiting and rebraiding usually occupying about three days.

This hair style, which is probably of great antiquity, is reminiscent of the head of Nefert in the Cairo Museum. The statue of Nefert, which belongs to the fourth dynasty of the old Kingdom of Egypt, is over five thousand years old. The hair style of Nefert, with its numerous short tight plaits, is, however, stated by Murray (1949) to be not real hair, but a wig.

FIG. 2.—Northern Sudanese woman with silk braided into her hair.

Alopecia of Northern Sudanese

Some degree of baldness is very common among women of the Northern Sudan, but only the more sophisticated think it worthy of mention to a doctor. Of the 12 patients who reported to hospital, five were aged 14 to 19 years, six were 20 to 40 years, and one was 50 years. The lesser degrees of alopecia are not infrequently encountered before the menopause. Severe alopecia is seen only in later life, when the condition is usually accepted without complaint.

In the process of plaiting, the hairs nearest the midline are more tightly stretched than those situated peripherally. There is a progressive thinning and atrophy of these hairs, which produces a diamond-shaped or rectangular area of baldness enlarging the central partings (Fig. 1). The area of baldness extends laterally and sagittally, sometimes leaving a few isolated hairs, too sparse or too short to be incorporated in the plait. No inflammatory changes have been seen in the

bald area of the scalp, even when the condition is actively progressing.

The women of the Northern Sudan are very reluctant to change their hair style, but three of the milder cases, in which the patients were persuaded to abandon the tight plaits, showed evidence of regrowth of hair within a month or two. As the alopecia progresses, the central bald area is naturally left undisturbed. In such advanced cases of long standing there is little or no regrowth of hair in the centre of the bald area.

Aetiology

The association of baldness with braiding of the hair in the Sudan is mentioned by the British explorer Bruce (1790). The Sittina of Shendi asked him whether he had medicine "to make her hair grow, or rather hinder it from falling off." He noted that "she was a woman scarce 40 . . . her hair was plaited in 10 or 12 small divisions like tails which hung down below her waist . . . with a kind of round cap of solid gold upon the crown of her head, all beat very thin." Bruce advised her to refrain from wearing the gold cap as the most likely cause of her falling hair.

None of the patients seen in the Khartoum Civil Hospital had any cap or gold ornaments on their scalps, the only covering being the thin cotton veil or "tobe." Mild seborrhoea capitis was present in one only of the 12 cases. In another the alopecia had been aggravated in the months following her two deliveries, but had not disappeared in the two-year interval between them.

There was no history of preceding fever or any evidence of tinea, syphilis, or the characteristic lesions of alopecia areata. One 16-year-old patient had a small simple goitre. Another, also aged 16, showed signs of mild hyperthyroidism. Otherwise the general health and nutrition of the patients were good.

The most striking features of the alopecia were the absence of inflammation, the distribution in the middle of the scalp where the stretching of the hair was greatest. and the improvement in those who changed their hair style. The most satisfactory explanation of the baldness is that it is the result of sustained traction on the hair exerted by the tight plaits.

In certain other types of baldness, trauma applied to the hair may be responsible for the condition. These are considered briefly.

Alopecia from Brushes and Combs

Savill (1958) has emphasized the importance of nylon brushes as a cause of alopecia. In the present shortage of natural hog bristle, nylon is being increasingly used in hair-brushes. In some of these the nylon bristle is not properly rounded off but is cut sharply across to leave a cylindrical end. There is then a risk of avulsion of the hair and, in time, thinning of the scalp. Only one example of this has been observed in the Sudan, and that was in an expatriate.

The Zande youth (Fig. 3) has a thin line of baldness running coronally across the head at the anterior margin of the hair. It appears to result from the trauma of the hardwood comb which he holds in his hand. The teeth of the comb are thrust horizontally back in the scalp and the tip of the handle is elevated. This causes the anterior hairs to be drawn into the apex of the triangle of the comb-teeth. These hairs are therefore subjected to greater tension than the rest when the comb is forced backwards and downwards.

Alopécie Liminaire Frontale

Sabouraud (1931), under the title "alopécie liminaire frontale," described a type of baldness forming a ribbon-like band across the front of the scalp from temple to temple. He stated that this was a rare condition of which he had seen only 10 or 12 examples in 30 years. The photograph illustrating this condition in Sabouraud's (1932) book shows a patient whose hair is drawn firmly back to form a tight bun in the occipital region. The bald area has appeared in the part of the scalp in which the roots of the longest hairs have been drawn taut in making the bun. Sabouraud was uncertain of the cause of the baldness, but the distribution closely resembles that of the Zande youth (Fig. 3).

FIG. 3.—Zande youth showing baldness from the habitual use of a hardwood comb.

Baliña (1932, 1937) described similar cases in South America. He expressed the view that the condition was caused by strong continuous traction of the hair, through the use of hair curlers. Further cases have been reported by Miskjian (1936), Kam, Light, and Walker (1949), and Savill (1952). More recently, Slepyan (1958) has described alopecia occurring in 24 young American girls as a result of traction from wearing pony tails. The baldness appeared at the roots of the tightly stretched hairs at the periphery of the scalp. Sometimes a fringe was worn. The baldness then appeared along the parting between the fringe and the pony tail at the roots of the tightly stretched hairs.

Alopécie Marginale Traumatique

Ribeiro (1937, 1938) described, as "alopécie marginale traumatique," a condition, occurring in negresses and mulattoes, of baldness above and anterior to the ears, which might subsequently spread. Casals (1938) reported cases from Cuba in the same type of patient, mainly over 40 years of age. Costa and Junqueira (1943), from Brazil, observed cases similar to those of Ribeiro. They stressed the role of curlers applied tightly to smooth out the characteristic kinkiness of negro hair. Anderson (1950) found examples in American negroes and negresses who had employed hot metal combs for the same purpose. Costa (1946) reviewed the condition of traumatic marginal alopecia and described certain variants on the general type. Ribeiro (1938), comparing his own cases with those of Sabouraud, pointed out that

European women use curlers simply to curl their hair. When the hair has been curled the instrument is removed and only re-employed intermittently. The negress and the mulatto, however, use the curler continuously to maintain a constant stretch on the hair, thereby concealing its kinkiness.

Kinkiness of the hair is regarded with disfavour by many races. Fig. 4 depicts the attempt of an Egyptian girl to disguise it. A gold clip has been placed coronally across the head and used as a fulcrum in pulling the hair tight with curlers. This has resulted in baldness over the temples and across the front of the scalp. It is not only hair curlers which cause such baldness. Spencer (1941) described the case of a 48-year-old negress who was bald, above and anterior to the ears, as a result of tight braiding.

FIG. 4.—Egyptian girl with alopecia due to a coronal gold band and tight curlers.

Allied Types of Alopecia

Sabouraud described a second condition associated with the wearing of a bun or "chignon." In "alopécie du chignon," areas of baldness develop at the level of lambda. The condition was observed in women of 30 to 50 years of age and was not associated with inflammation of the scalp. The area of baldness occurred where the bun rested on the scalp. The most probable cause would appear to have been the traction and twisting of the hair necessary to form and maintain the bun. A variant is the ophiasis celsi, or snake-like alopecia, which is found in women with a circumferential coiling of the hair. Examples of this condition have been reported by Costa (1946) and Omens *et al.* (1954, 1955). The hair is pulled tight in a curved line round the periphery of the scalp, and the baldness develops along this line.

Traction Alopecia

All these forms of alopecia, despite their differing distribution, are associated with traction on the hair. The multiplication of anatomical descriptive terms disguises the central fact that traction is common to them all. Permanent baldness often results from long-continued traction. The hairs may recover, however, if traction is promptly stopped by altering the hair style. The term "traction alopecia," as recommended by Slepyan, should be applied to this group of conditions.

European women do not often suffer from this type of baldness, certainly not in its extreme form. They seldom subject the hair to such intense traction, and they change their hair style from time to time. They are, as Ribeiro pointed out, very sensitive to the slightest sign of baldness and will rearrange their hair style to hide it. Traction alopecia will be encountered, therefore, most often in non-Europeans.

Summary

Women of the Northern Sudan develop baldness over the centre of the scalp in association with tight plaiting of the hair. The condition is the result of traction on the roots of the hair. Other examples of traction alopecia are quoted, and the importance of relieving the traction is emphasized in order to prevent permanent loss of hair.

I am grateful to Dr. Ahmed Ali Zaki, Director of Medical Services, Ministry of Health, and to Sayed Hassan Ali Abdalla, Permanent Under-Secretary, Ministry of Interior, Republic of the Sudan, for permission to publish this paper.

REFERENCES

Anderson, J. W. (1950). *Arch. Derm. Syph. (Chicago)*, **62**, 910.
Baliña, P. L. (1932). *Rev. argent. Dermatosif.*, **16**, 599.
—— (1937). Ibid., **21**, 21.
Bruce, J. (1790). *Travels to Discover the Source of the Nile*, **4**, 532. Robinson, London.
Casals, D. A. (1938). *Rev. Cienc. méd. (Habana)*, **1**, 133.
Costa, O. G. (1946). *Brit. J. Derm.*, **58**, 280.
—— and Junqueira, M. A. (1943). *Arch. Derm. Syph. (Chicago)*, **48**, 527.
Kam, J., Light, R. C., and Walker, A. E. (1949). Ibid., **60**, 905.
Miskjian, H. G. (1936). Ibid., **33**, 750.
Murray, M. A. (1949). *The Splendour that was Egypt*, p. 122. Sidgwick and Jackson, London.
Omens, D. V., Omens, H., and Holt, L. (1954). *A.M.A. Arch. Derm.*, **69**, 751.
—— —— —— (1955). Ibid., **71**, 749.
Ribeiro, H. (1937). *Brasil-méd.*, **51**, 1267.
—— (1938). *Ann. Derm. Syph.*, **9**, 501.
Sabouraud, R. (1931). Ibid., **2**, 446.
—— (1932). *Diagnostic et traitement des Affections du cuir chevelu*, p. 399. Masson, Paris.
Savill, A. (1952). *The Hair and Scalp*, 4th ed., p. 148. Arnold, London.
—— (1958). *Brit. J. Derm.*, **70**, 296.
Slepyan, A. H. (1958). *A.M.A. Arch. Derm.*, **78**, 395.
Spencer, G. A. (1941). *Arch. Derm. Syph. (Chicago)*, **44**, 1082.

The dramatic decline in the incidence of tuberculosis in all but the oldest age groups during the past few years is reflected in a report on the future of the chest services prepared by the Standing Tuberculosis Advisory Committee, and now commended by the Minister of Health to the attention of hospital authorities. One of the main recommendations is that in new hospitals beds should be available for diseases of the chest, some of them being set aside for cases of tuberculosis. Similar provision should be made in existing general hospitals where possible; otherwise existing suitable sanatoria and chest hospitals could be used as chest departments of near-by hospitals or run in close association with them. After recommending that the chest physician should be a member of the staff of a general hospital, with a primary duty to tuberculosis patients, the report emphasizes that it is important that he should work closely with the medical officer of health on epidemiological and preventive implications, and continues, "The end of the epidemic prevalence of tuberculosis in our community can now be seen as an attainable object, although it may be many years ahead." The report continues: "The normal pattern of the future should be that appointments in chest diseases should be to the staffs of general hospitals, the chest clinic being integrated into the general out-patient department of the hospital and sharing the general services of the department. Only if some such policy is adopted will young doctors considering their future careers see in diseases of the chest the prospect of continuing work during their lifetime, even though the decline in tuberculosis continues."

Preliminary Communications

Storage of Red Cells for Blood-grouping after Freezing in Liquid Nitrogen

Use of Sucrose to Protect Against Haemolysis

An increasing number of laboratories find it necessary to keep a panel of erythrocytes of known antigenic structure for blood-grouping work. Long-term storage of such cells has been made possible by freezing after the addition of glycerol (Chaplin and Mollison, 1953). However, care must be taken in the gradual adding and withdrawal of the glycerol, as otherwise considerable haemolysis may result. In particular, recovery of the cells from the glycerol is a rather tedious procedure.

An alternative is very rapid freezing in liquid nitrogen, storage at a suitably low temperature, and equally rapid thawing. Valuable work has been done by Meryman and Kafig (1955a, 1955b) along these lines, concerned with preserving blood for transfusion purposes. The present note describes a simple method suitable for keeping the small quantities needed for serological work.

PROCEDURE

Preparation.—Blood is anticoagulated with E.D.T.A. in the proportion of 1 mg. per ml. Shortly before freezing, one volume of 40% (w/v) sucrose solution is added to two volumes of blood. A very fine-pointed Pasteur pipette is then filled with the blood–sucrose mixture.

Freezing.—Not more than four or five test-tubes of about 15-ml. capacity are filled one-third full of liquid nitrogen. (This substance is quite easily handled, being poured from the storage vessel into the tubes with the aid of a small funnel. It will boil vigorously for a few seconds and then more quietly.) Blood is dropped slowly into the tubes from the pipette, each drop freezing apparently instantaneously as it enters the nitrogen. When a sufficient quantity (say 20 drops) has been added in each tube, the frozen blood and the small quantity of nitrogen now remaining is decanted into small storage tubes. (The glass tubes can safely be held at their upper ends with bare hands.) The storage tubes, preferably already labelled, are tightly plugged with cotton-wool and placed in the storage cabinet at once, the remaining nitrogen boiling off at storage temperature.

Thawing.—The selected tubes are removed from the storage cabinet and, without delay, the cotton-wool plugs are removed and the frozen blood is tipped into about 5 ml. of saline at 45° C. The tube containing the saline is at once thumb-stoppered and inverted several times, the blood thawing within one or two seconds. The cells may then be centrifuged and resuspended in saline or test serum as required for use.

PRE-TREATMENT OF BLOOD

Various anticoagulants were tried and E.D.T.A. was found to give the best recovery of intact cells (20–30% haemolysis when thawed immediately after freezing). Acid citrate–dextrose showed an improvement on this figure, with 10–20% haemolysis, but this is due to the presence of dextrose. Meryman and Kafig (1956a), using a rather complex device to decrease droplet size, have claimed losses of only 2–3% after the addition of 7% dextrose to the blood. By the present method, the best result, using dextrose, was about 10% haemolysis when one volume of 40% (w/v) dextrose was added to four of E.D.T.A. blood (giving a final concentration of 8% dextrose). Adding to two volumes of blood one of 40% (w/v) sucrose proved a considerable improvement, giving a loss of 4–6% when used as described above. The sugar concentration has a definite optimal level, recovery falling off quite sharply if the concentration be changed either way.

STORAGE

The ordinary laboratory deep-freeze at −10 to −20° C. is not cold enough for this purpose. We have, however, stored the frozen blood in CO_2 snow for a few weeks. The amount of haemolysis in the thawed blood appeared to increase from the original 5% to about 10% after the first day or two of storage, but then remained at this level for the rest of the short test period. It is possible that the CO_2 vapour may be the cause of this immediate deterioration.

CO_2 snow is obviously impracticable, as it needs such frequent replenishment and, regrettably, refrigerators working at a similar temperature are at present very expensive. Further work is necessary to ascertain the optimum (or maximum effective) temperature which will preserve the cells; it may well be that −40° C. is sufficient, and refrigerators working to this temperature are much less costly.

A great saving in storage space and time taken in freezing can be effected by freezing the blood in larger quantities (several hundred drops) in 25-ml. universal containers, replenishing the nitrogen from time to time. When thawed blood is required, a bunch of frozen droplets is picked out of the container with a pair of long forceps (kept at storage temperature) and dropped into warm saline as before.

GROUPING PROPERTIES

Cells representing A, B, C, D, E, $\bar{c}$, M, N, K, and Fy^a groups showed unimpaired reactions after freezing and thawing by the above method.

Thanks are due to Dr. A. Bracken, of the British Oxygen Company, for arranging for a supply of liquid nitrogen and CO_2 snow.

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REFERENCES

Chaplin, H., and Mollison, P. L. (1953). *Lancet*, **1**, 215.
Meryman, H. T., and Kafig, E. (1955a). *Proc. Soc. exp. Biol. (N.Y.)*, **90**, 587.
—— —— (1955b). Naval Med. Research Inst. Project NM000. 018.01.10.

Members of the Association of British Pharmaceutical Industry, in response to an appeal put out by the "Save the Children Fund," have donated essential supplies for victims of the recent earthquake in Agadir. Among the medical supplies flown out were antibiotics, sulphonamides, various types of iron and vitamin tablets, and numerous other pharmaceutical products, including sera.

Reviews

MODERN PATHOLOGY

Modern Trends in Pathology. Edited by Douglas H. Collins, O.B.E., M.D.(L'pool.), F.R.C.P.(Lond.). (Pp. 334+x+12: illustrated. 70s.) London: Butterworth and Co. (Publishers) Ltd. 1959.

The "Modern Trend" series has now become well established, and each new volume is awaited with pleasurable anticipation. The title of the present volume may be slightly misleading, inasmuch as the editor has had to choose some of the very highly specialized fields in order to indicate the trends of research in pathology. Nevertheless, if this book is read carefully, there is a wealth of information on new thinking in pathology which is exciting and stimulating.

Sir Roy Cameron's chapter on the injured cell, including both the general form of cell mitochondria and the more specialized reactions of cells—e.g., the cells of the pancreatic islets—brings to light the detailed investigation on structure, particularly of granules in cells, and the author asks a pertinent question as to whether they are really part of the cell metabolism, or whether they have a life history of their own. This is carried a stage further by the techniques of phase contrast microscopy, and the beautiful preparations from normal tissues (particularly in bone marrow), and the very different tumour cells in the chapter by Professor Pulvertaft.

It is difficult, however, to review the book in piecemeal fashion, and each chapter stands by itself as an example of a survey of present knowledge done by a particular author. The present-day investigation of cancer of the liver and cancer generally in Africa shows the influence which geographical pathology has on present-day thinking. The adrenal cortex, of course, is given considerable prominence, and the discussion on the hormones produced by the adrenals, together with their influence on disease, though limited to more recent advances, is very stimulating.

The influence of the editor is indicated in the uniformly well-written chapters and the high standard of production. The photomicrographs are exceedingly clear and well-proportioned, and the bibliography of each chapter is more than adequate. This volume is essentially one for the cytologist and histopathologist, but there is enough general pathology in such matters as the production of antibodies and hormones and the neurotropic viruses to attract pathologists with wider interests. This book does succeed in exemplifying the new dynamic approach which has developed in pathology, and which has so encouraged the younger research workers.

A. G. SIGNY.

ATELECTASIS

Die Streifenatelektasen der Lunge. By Friedrich Heuck. M.D. *Zwanglose Abhandlungen aus dem Gebiet der Normalen und Pathologischen Anatomie.* Edited by Professor Dr. W. Bargmann and Professor Dr. W. Doerr. Part 7. (Pp. 108+xiii; illustrated. DM. 25.60.) Stuttgart: Georg Thieme Verlag. 1959.

This monograph by Dr. Friedrich Heuck on "plate-like" or linear atelectasis of the lung is a very comprehensive work, involving a good deal of research, especially of a radiological nature.

The whole subject of atelectasis, which means incomplete expansion of the lung, has been found to be confusing, for the term should strictly be confined to the congenital condition in which the lung fails to change from the foetal to the fully expanded state. One should therefore speak in terms of acquired or congenital atelectasis. The former, which concerns us here, is usually divided into compression atelectasis and bronchial obstruction. The essential features in the formation of plate-like or linear atelectasis, which occurs mainly at the bases of the lung, is said to be due to the absence of collateral ventilation through shallow breathing. As a result of his post-mortem findings, Fleischner describes this condition as caused by obstruction of a segmental bronchus causing collapse of a portion of the lobe, with consequent retraction of the segment. The surrounding healthy alveoli undergo compensatory dilatation, and the affected area on collapse shows a plate-like or linear shadow, seen in the horizontal position on a chest radiograph. Occasionally the shadow is somewhat broader and sometimes a linear shadow may merge into the diaphragm, which may at first glance be missed on the radiograph. These shadows are most commonly unilateral. Occasionally, where the linear shadow approaches the periphery, there may be an interlobar effusion which may be difficult to diagnose.

The author of this book has investigated 15,130 radiographs of the chest over a period of four years and has encountered 174 cases of plate-like atelectasis in various conditions. In diseases of the lungs, including pulmonary infarction, emphysema, bronchiectasis, tuberculosis, and new growths, he found 58 cases; in diseases of the heart and circulation, 68 cases; and in upper abdominal diseases, with or without ascites, 11 cases. I have myself found several cases of plate-like atelectasis in the lungs in cases of systemic lupus erythematosus, with or without pleural effusion.

Dr. Heuck discusses problems in differential diagnosis, including pleural involvement and consolidation. He states that these linear atelectases may be short- or long-lived, when they leave behind a fine scar. They may precede or follow diseases involving a major portion of the lung.

Those interested in the various aspects of atelectasis and this specialized form so comprehensively described will benefit enormously from this monograph, which is beautifully illustrated with excellent radiographs, supplemented by tomographs and bronchographs where necessary. There is a most extensive bibliography, which, though it refers in the main to German literature, none the less includes references to world literature.

PHILIP ELLMAN.

(This review was written shortly before Dr. Ellman's death.)

BIOLOGICAL SCIENCES AND THE SKIN

Progress in the Biological Sciences in Relation to Dermatology. Edited by Arthur Rook, M.D., M.R.C.P. (Pp. 480+xv; illustrated. 84s.) Cambridge University Press. 1960.

Dr. Rook was to be congratulated on having attracted to the subject of dermatology the first of the series of symposia on progress in biological sciences at Cambridge. He has now edited the work presented and the discussions in a most able fashion.

The collection of 17 papers contains important information on research that is directing advances in the understanding of the mechanism of disease and of its treatment. The papers are presented by masters in each subject and in such a manner as to be intelligible

to clinicians who are not necessarily or often trained in the basic sciences. The papers are all fascinating and instructive and cover the fields of melanogenesis and of cutaneous innervation. There are excellent contributions on immunology and sensitization and on the pharmacology of vasodilator drugs. Histochemistry, inflammation, bacteriology, and carcinogenesis are discussed in relation to the skin, and there is a series of papers on psychological mechanisms. Those who were privileged to attend the course will regret that these edited proceedings do not include the attractive paper by Dr. Gale on the bacterial cell even though it had appeared elsewhere, but that is the only criticism to be offered.

Such a course and this record of the contributions are of interest not only to dermatologists. It is understood that further similar courses are to be arranged at appropriate intervals, and that is welcome news. The production by the University Press is excellent in every way.

J. T. INGRAM.

CHILDREN'S ABDOMINAL PAINS

The Child with Abdominal Pains. By John Apley, M.D., F.R.C.P. (Pp. 86+vii. 12s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

This short monograph is excellent. It is a model of clarity and common sense and gives a detailed account of how the common and often difficult problem of abdominal pain in childhood may best be tackled. There must be few surgeries and children's out-patient departments where the problem is not encountered almost daily. Dr. Apley shows that there is no easy way out and certainly no quick way. Dealing with such children and their parents is a time-consuming process, but one which well repays the time spent.

The myths of abdominal migraine and epilepsy are exploded, and, though not a therapeutic nihilist, the author concludes that medicines play little part in treatment. It is in keeping with general paediatric experience that only 7% of the children with abdominal pain had any organic cause for the pain; in half the origin was in the alimentary tract and in half in the renal tract. An interesting finding was the high incidence of abdominal pain in the relatives of affected children.

The monograph deserves a better binding; otherwise it is well produced and only two mistakes were found—the mis-spelling of Brennemann's name and the omission of "not" in a quotation from Hill on page 71. There is an excellent bibliography. The lay-out is so clear, the headings so plain, and the summaries at the end of the chapters so adequate that the index is really unnecessary.

Family doctors and paediatricians alike may read this book with pleasure and profit; it is commended without reservation.

WILFRID GAISFORD.

Written in English, and firmly based on the standard British pharmacopoeias, the *Ceylon Hospitals Formulary 1959* is compact, compendious, and helpful. The official names of drugs are used throughout and proprietary equivalents given in a table at the end. Doses are in the metric system, but are given also in the apothecaries' where this has been conventionally used in the past. The formulae are arranged on a pharmacological basis, and Professor S. W. Bibile, of Ceylon University, introduces each section by an instructive account of the drugs in it. Published by the Ceylon Department of Health, the *Formulary* is printed on good paper.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Manual of Skin Diseases. By Gordon C. Sauer, M.D. (Pp. 269+xvii; illustrated. 70s.) London: Pitman Medical Publishing Co., Ltd. 1960.

New Methods of Studying Gaseous Exchange and Pulmonary Function. By Alfred Fleisch, M.D. Translated by Charles Corsi. (Pp. 116+xiv; illustrated. 46s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Elongation Treatment of Low Back Pain. By George H. Hassard, M.D., and Charles L. Redd, B.S., P.T. (Pp. 78+xvi; illustrated. 36s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Paediatric Prescriber. By Pincus Catzel, M.B., B.Ch. (Rand), M.R.C.P.Ed., D.C.H., R.C.P.&S.(Eng.), assisted by S. Cohen, M.P.S.(S.A.) (Pp. 244+xvi. 15s.) Oxford: Blackwell Scientific Publications. 1960.

Surgical Philosophy in Mass Casualty Management: With Detailed Notes on Practical Care. By Warner F. Bowers, A.B., B.Sc., M.D., M.S., Ph.D., and Carl W. Hughes, A.B., M.D. (Pp. 204+ix. 54s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

British Medical Bulletin. Volume 16, No. 2. *The Thyroid Gland.* (Pp. 89–174; illustrated. 20s.) London: British Council Medical Department. 1960.

Electrophoresis in Physiology. By Lena A. Lewis, Ph.D., LL.D. With a chapter on *Immunoelectrophoresis* by M. D. Poulik. Second edition. (Pp. 120+v; illustrated. 44s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Primary Tumors of the Calvaria: With Special Consideration of the Clinical Problems. By Franklin Jelsma, M.D. (Pp. 116+x; illustrated. 56s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Mitra Operation for Cancer of the Cervix: Extraperitoneal Pelvic Lymphadenectomy and Radical Vaginal Hysterectomy. By Subodh Mitra, M.B.(Cal.), Dr.med.(Berlin), F.R.C.S.(Edin.), F.R.C.O.G., F.A.C.S., F.N.I. (Pp. 93+xix; illustrated. 48s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Dreams and Personality Dynamics. Edited by Manfred F. DeMartino, M.A. (Pp. 377+xvii. 84s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Electrohysterography: The Electrical Activity of the Human Uterus in Pregnancy and Labor. By Saul David Larks, B.S.E.E., M.S.(E.E.), Ph.D. (Pp 123+xiii; illustrated. 46s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Diagnosis and Treatment of Diseases of the Trachea and Bronchi. By Herman J. Moersch, M.D., and Howard A. Andersen, M.D. (Pp. 108+vii; illustrated. 34s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Photography in Medicine. By Arthur Smialowski and Donald J. Currie, M.D., M.Sc., F.R.C.S.E., F.R.C.S.(C.), D.S., F.A.C.S. (Pp. 330+xviii; illustrated. £5 16s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Studies on Vertebrate Neurogenesis. By Professor Santiago Ramon y Cajal. Translated by Lloyd Guth, M.D. (Pp. 432+xiv; illustrated. £5 8s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Laboratory Identification of Pathogenic Fungi Simplified. By Elizabeth L. Hazen, Ph.D., and Frank Curtis Reed. Second edition. (Pp. 150+xv; illustrated. 60s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Practical Neurological Diagnosis. With Special Reference to the Problems of Neuro-Surgery. By R. Glen Spurling, M.D. Sixth edition. (Pp. 284+xviii; illustrated. 54s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Extremities. By Daniel P. Quiring, Ph.D. Second edition, revised and edited by John H. Warfel, Ph.D. (Pp. 120; illustrated. 24s. 6d.) London: Henry Kimpton. 1960.

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MEDICAL DEMOCRACY AT WORK

The Annual Representative Meeting at Torquay lasted four whole days. Thousands upon thousands of words poured into the microphone and out of the loudspeakers. Under Dr. Arthur Beauchamp, the Chairman of the R.B., the platform was alert to every step in the complicated moves of doctors in the role of democrats. Dr. S. Wand, the Chairman of Council, was at hand to expound, guide, and intervene. The B.M.A. staff, under the direction of Dr. D. P. Stevenson, the Secretary, kept the whole machine moving so efficiently that no one could guess just how complicated it all was and what an enormous amount of detailed planning had been necessary. Just below the platform representatives of the national press sat patiently waiting for a good story to break, and the *B.M.J.* reporters recorded faithfully for the *Supplement* the good, the bad, and the indifferent, so that the members of the B.M.A. at large should be informed in sufficient detail just what its representatives had said and resolved. Behind the scenes at Torquay and in London the *B.M.J.* staff was editing, checking, keeping constant the flow of copy to the printer, and hoping that at least no one's name was spelt incorrectly and that all surgeons who spoke were designated as "Mister." The pattern is pretty well the same year after year, and the modifications introduced after decades of experience have made a machine that runs smoothly and more or less to time. And now the preparations for the next annual meeting—in New Zealand—are well in hand.

When Dr. W. H. N. Angus, of Southampton, urged the Council to take steps to remedy "the disgusting state of certain beaches" he started a debate that was carried on vigorously in the national press and forced itself upon the attention of Parliament. The debate has compelled central and local authorities to look once again at the unpleasant facts of pollution of seas and rivers. This was but one of the many public health problems that came before this year's R.B. The Council has been asked to look again at the question of "making recent medical evidence of clean health a prerequisite for the admission of immigrants to the United Kingdom." On a motion from Buckinghamshire, local authorities are to be urged to encourage active immunization against tetanus, especially among schoolchildren. Another motion that won the day, also from Buckinghamshire, asked the Ministry of Health to produce standardized cards for recording the various immunizations. The "pasteurization" of imported egg products to control food infection was still one more public-health procedure advocated by the R.B. For those who have felt that in the past the Representative Meeting has been too preoccupied with payment for professional services, this emphasis on measures to protect the public health will be pleasing. And it must have gratified our colleagues in the public health service that it was a general practitioner, Dr. R. M. S. McConaghey, who successfully moved a resolution that the B.M.A. Council should press for an immediate re-examination of their salaries.

With the working parties already busy looking into the implications of the proposals of the Royal Commission, there was much less stress than usual on remuneration. What appeared to be an ambiguity about the retrospective payment of general practitioners according to the Pilkington proposals was resolved in the light of open debate. The R.B. paid close attention to the reasoned arguments by Dr. J. A. L. Vaughan Jones in favour of providing some monetary compensation to the chief officers of the Association, who make considerable financial sacrifices in their performance of voluntary work for the B.M.A. Dr. Vaughan Jones spoke as chairman of a special committee set up by the Council to examine this difficult and delicate matter. That it came up at all for debate is yet another illustration of the altered position of the professions in Britain to-day. The cost of living and education combines with taxation to make it more and more difficult for doctors to make a free contribution not only to their own profession but also to the public life of the community in which they live. The debate showed that the R.B. was deeply concerned about two things: the financial loss incurred by the B.M.A.'s chief officers, and the desirability of preserving the principle of voluntary service. The whole matter is to be considered afresh.

But at least one conclusion can be drawn now—the Association does not suffer because its chief officers and chairmen of committees are unpaid. The evidence is their activity, and fruitful activity. To single out anyone is obviously invidious. If the *Journal*—from its relatively detached position in the structure of the B.M.A.—drew attention to the progressive improvement over the past years in the publishing side of the Association's activities under

the over-all guidance of the Journal Committee under Dr. J. G. M. Hamilton it might be accused of sycophancy—the most ignoble of all human weaknesses. In another leader we refer to the quite remarkable and shrewd thrusts of the Private Practice Committee that have given members of the B.M.A. benefits which, in terms of enlightened self-interest, are, we believe, unequalled in any other medical association. They are visible, tangible, and prudential. The Organization Committee believes in the policy of "the follow through." The greater the difficulties before it, the greater seems its determination to break through them. It is giving a lot of attention to planning—and much of its planning is concerned with the welfare of the younger doctor. If the Hastings Wine Club brings solace to the older member, the *Hospital Gazetteer*, now about to be published, is designed to let the young hospital doctor know where he can get a fair and square deal—and it will stimulate hospital authorities to make sure that the deal is dealt. The "subject of the year" was a courageous concept—courageous if only for the fact that medicine is now more and more a subject of special studies which uneasily lend themselves to the method of peripatetic discourse. The Junior Members Forum, too, has provided what was needed.

In his report to the R.B., the Chairman of the Organization Committee, Dr. R. G. Gibson, referred to the fact that during the year the Singapore, Malayan, and Pakistan Medical Associations were about to become affiliated to the B.M.A. Professor D. E. C. Mekie (Chairman of the Overseas Committee) told the R.B. that Nigeria, too, would be going in the same direction. The Australian Branch is to become a medical association affiliated to the B.M.A. The most moving occasion of the meeting of the Representative Body was provided by those chosen to make their observations to the R.B. from the platform, beginning with Dr. Alan E. Lee, of Australia. The ideal of a commonwealth free from the degrading distinctions of race, creed, or colour was, indirectly, expressed by Dr. W. K. Chagula, of Uganda, who appealed to Representatives, "their children, and their relatives, who have been or are contemplating the possibility of going to work in this developing Africa, not to slam the door against that possibility now."

The two set pieces of any R.B. are the reports of the two formidable autonomous committees of the Association—the General Medical Services Committee and the Central Consultants and Specialists Committee. In his account of the year's record of the former, Dr. A. B. Davies kept the meeting on a straight course in one of the most controversial items before it—deputizing arrangements. A good and properly organized deputizing service, he said, had nothing to fear. "The profession would have full control through local medical committees." Much of his report bore upon the need for general practitioners for closer contact with hospitals. The G.M.S. Committee, he observed, wanted properly equipped modern obstetric departments in hospitals, and an adequate number of general-practitioner beds. A motion was carried in favour of making fully available to general practitioners such ancillary hospital services as radiology, pathology, cardiography, and physiotherapy; and another motion, also carried, urged that the number of clinical assistant posts for general practitioners in hospitals be increased. That there should be no change of use of a hospital without the consent of the local profession, and that the Minister of Health should give "special consideration to the preservation and improvement of general-practitioner units" was successfully moved by Dr. G. P. Wallace (of Guildford).

The sad state of British hospitals to-day was underlined in Mr. H. H. Langston's account of his stewardship as Chairman of the C.C. and S. Committee. "We have never said we want more beds," he said. "What we want is up-to-date hospitals." There were still existing "large, gloomy wards and 30 to 40 beds with one bathroom, horrible sanitary arrangements, and no facilities for the carrying out of sterile procedures in the wards." He drew attention to the overcrowded out-patient departments and long waiting-lists. What he said was echoed by many other speakers, and Mr. C. Remington-Hobbs made the necessary point that "the thinking should not be confined to the design of hospitals for the present time, but should have regard to requirements that would exist at the end of the century and the main part of the next."

The fact that after ten years' experience of the N.H.S. the Representative Body is more apprehensive than ever of a whole-time salaried medical service, and of the relationship of the State to the profession, was shown in a number of ways. The renewed plea for drugs for private patients was one of these. Dr. A. B. Davies opposed a motion that the executive council should pay (for one week a year) for a locumtenent on the grounds that it "would be taking a very important step in the direction of a State-salaried service." A motion that whole-time consultants should be allowed limited private practice, and that part-time consultants should be offered whole-time contracts, was regarded as "a dangerous move towards a whole-time State-salaried service." That there is a deep undercurrent of unease about this

was shown by the intent way in which the R.B. followed Dr. J. B. Wrathall Rowe's closely argued case about the exact status in law of the G.P. in the N.H.S. The R.B. also showed much anxiety about what they thought might be an encroachment on traditional medical ethics with the proposed slight relaxation of the rules on anonymity. Mr. J. R. Blackburn said : " In recent years there has been a gradual change in B.M.A. policy on ethics and I am not happy about it. We are now asked to relax our rules." The R.B. finally passed the following motion: " That this meeting deplores the fact that the report of Council on Advertising and the Medical Profession fails to condemn effectively medical practitioners who co-operate with the lay press in the publication of medical articles of a sensational nature." This was moved by Dr. K. W. Beetham, who held up to the meeting a copy of the weekly periodical *Reveille* containing an article on cancer, and heralding another one on rheumatism. " There is nothing in this which could be regarded as unethical," he said, " because the ethical rules are made for ' Joe Soaps ' and not for these practitioners in the top flight."

We have touched upon only a few of the subjects for debate at Torquay. We hope that members not present will read the full report of the proceedings in the *Supplement* of June 25 and July 2, and in doing so perhaps remember that the discussions and outcome from them in the form of resolutions defining the policy of the B.M.A. are the result of a year's hard work by B.M.A. committees and their chairmen, by Council and its Chairman, who at much cost to themselves do this unpaid work as a voluntary contribution to the welfare of the medical profession.

MATERNAL MORTALITY

What criteria should be used to judge the quality of the much discussed, if not criticized, maternity services of this country ? The views of consultant obstetricians, general-practitioner obstetricians, and midwives tend to be coloured by what the service offers them in the way of facilities to practise midwifery. Those who administer various aspects of the service also naturally have their own particular interests. The patients themselves usually base their assessment of the service on the day-to-day conveniences and the physical and mental comforts which they experience in clinic, surgery, and childbed. They tend to overlook the fact that child-bearing is still a matter of life and death for them and their babies, and, if a choice has to be made, that it is worth sacrificing a bunch of flowers, a cup of tea, and even an extra kind word to preserve life and health. The steep fall in the maternal death rate during the last thirty years can give even the members of the medical and nursing profession a sense of false security.

The comparative rarity of maternal deaths in any one hospital or area has, in recent years, resulted in local standards of practice being judged by the perinatal mortality. Thus some of the larger maternity hospitals base their regularly held staff meetings on the stillbirths and neonatal deaths occurring in the previous month. Such staff conferences, popular overseas for several years, are still in this country the exception rather than the rule. And yet, as will be testified by all those with experience of them, they have much to offer by way of education and by way of improving the results of any hospital. Such conferences, as the Cranbrook Report[1] suggested, could well be extended to cover the domiciliary midwifery within a hospital's area of influence, thus giving general practitioners, obstetricians, and hospital and district midwives the opportunity to meet and discuss clinical problems which arise both without and within hospital.

Despite the shift of emphasis to the child, it remains necessary to recognize that the number of maternal deaths throughout the country is still not insignificant, and nearly every one means the loss of a healthy young woman on whom a whole family structure depends. Moreover, for every death there are many near-deaths which are not shown in published statistics. Even when it does not kill, abnormality at childbirth often leaves permanent disability of varying degree. That many more women could escape death or disablement is strongly suggested in a new report about to be issued by the Ministry of Health.[2] This follows the lines of a previous publication[3] and summarizes the results of confidential inquiries into the maternal deaths occurring in England and Wales during the years 1955 to 1957. During this three-year period 1,112 deaths were notified to the Registrar-General as being directly caused by pregnancy and childbirth, and 861 (77%) of these became available for expert assessment. More than 50% of the missing cases were deaths from toxaemia, abortion, and ectopic pregnancy. During the same years there were also 368 deaths registered as being caused by other diseases occurring in pregnant women—" associated deaths "—and, of

[1] Ministry of Health. *Report of the Maternity Services Committee*, 1959, p. 87, para. 314. H.M.S.O., London.
[2] Ministry of Health. Reports on Public Health and Medical Subjects, No. 103, *Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1955-57*, 1960, in press. H.M.S.O., London.
[3] —— Reports on Public Health and Medical Subjects, No. 97, *Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1952-54*, 1957. H.M.S.O., London. See leading article, *Brit. med. J.*, 1957, **2**, 280.
[1] *Brit. med. J.*, 1956, **2**, 932.

these, 339 (92%) were the subject of confidential inquiry.

Like its predecessor, this report contains valuable information covering a wide range of subjects, makes fascinating reading, and has many lessons to teach. As might be expected, the total number of maternal deaths was less than for the period 1952–4 covered by the first report, and this despite an increase in total births. The decrease was proportionate among all causes of death except haemorrhage, pulmonary embolism, and sepsis. There were relatively and absolutely more deaths from sepsis and embolism but an improvement in the figures for haemorrhage. This improvement showed mainly in the condition of postpartum haemorrhage associated with retention of the placenta, and is probably explained by better care of the third stage in general, by the freer use of ergometrine, and by the work of obstetric flying-squads. Despite the fewer deaths in this particular group, the inquiries led to the conclusion that 61% of deaths from all types of haemorrhage, and 50% of deaths from postpartum haemorrhage, could have been avoided by referral of patients at risk to hospital for delivery, by prompt and adequate blood transfusion, and by earlier recognition of the seriousness of a situation. In only 21% of the women who died from haemorrhage had any attempt been made to assess the presence of pre-existing anaemia, or to have a haemoglobin estimation carried out at any time during pregnancy.

Toxaemia of pregnancy remained the leading killer, accounting for 171 (22%) of deaths: 90 (53%) of these could have been prevented by conscientious and efficient antenatal care, with admission of the patient to hospital at the first sign of pre-eclampsia.

The next three most important causes of maternal death were pulmonary embolism (17%), abortion (16%), and haemorrhage (14%). This is a remarkable change, and the fact that pulmonary embolism now ranks second is a challenge to all those concerned with obstetrics. It should be noted that in the great majority—114 out of 157 cases—the fatal embolism occurred after vaginal delivery, and in half of them the occurrence of deep thrombosis or a small embolism had given warning of the possibility of catastrophe. Except when a predisposing condition was ill-managed the assessors did not classify any of these embolic deaths as avoidable, because there is, as yet, no general agreement on the appropriate treatment. Nevertheless, it may be significant that among the 157 fatal cases only 8 had received any sort of anticoagulant therapy. Not only is embolism now the second most important cause of maternal death; deep thrombosis is a common cause of persistent incapacity. There is clearly an urgent need for the investigation of this problem. Apart from raising the question of the place of anticoagulants, the report gives one lead by showing that the risk of embolism rises with maternal age and to a lesser extent with parity.

One hundred and eighty-four women died after caesarean section, and it is calculated that the mortality rate for this operation in England and Wales was 3.5 per thousand—that is, approximately 8 times higher than the total maternal mortality rate at the time. Inevitably the operation was often done in desperation for serious complications of pregnancy. Nevertheless, the majority of the deaths resulted from haemorrhage, sepsis, and embolism, and some, at least, were clearly avoidable. Certain women suffering from placenta praevia died, the report suggests, because of failure to transfuse with blood and because of inexperience of the surgeon; sometimes a consultant was notified too late.

It will probably surprise those who have emphasized anaesthetic hazards in recent years to learn that rupture of the uterus killed more women (33) than did anaesthesia (31). There is a tendency to regard this accident as a thing of the past, and it is salutary to see a special section of the report devoted to it. For every fatal case of ruptured uterus there must be many non-fatal ones. Another special chapter deals with sudden death in labour, of which there were 44 cases, with a variety of causes headed by the still unsatisfactory term "obstetric shock." Even these sudden and unexpected deaths often had a background of avoidable factors.

Throughout the report it is made clear by illustrative cases that the criteria used in assessing avoidability were both humane and liberal. Only gross neglect of accepted standards of care and overwhelming evidence of mismanagement justified labelling a death as avoidable. On this basis 353 (41%) true maternal deaths and 57 (16.8%) associated deaths could have been prevented. Sometimes more than one avoidable factor was present and responsibility was shared, but the fault was ascribed to domiciliary services alone in 121 cases, to hospital services alone in 75 cases, and to the patient alone in 55 cases. Rarely was the administration to blame. "Most of the avoidable factors were the responsibility of individuals. . . ." This shows even among associated deaths. Women dying from cardiac failure had not even had their heart examined despite giving a history of rheumatic fever. Known cases of mitral disease were booked for delivery at home and received no special care or antenatal supervision.

But this report is not concerned to attach blame except in so far as to point the way to the avoidance of unnecessary tragedies in the future. The emphasis is on such basic matters as intelligent antenatal care, designed to suit the individual case rather than to

satisfy a routine, and on the selection of cases for home and hospital delivery. Here it may be noted that the figures in one table suggest that, although parity alone raises the hazards of childbearing, age is an even more important factor. Thus it would appear that the woman of 35 having her second or third baby is at greater risk than the woman of 25 having her fourth or fifth baby.

Merely by conscientious and wise application of knowledge available at the time, the number of maternal deaths occurring in England and Wales during 1955–7 could have been nearly halved. Since that time the maternal death rate has fallen: in 1958 the figure for England and Wales was less than 0.4 per 1,000. Can it be lowered further? Yes, says the report, a figure of 0.1, or at the most 0.2, is immediately attainable. By 1953 the number of true maternal deaths in England and Wales had fallen to approximately 500 per year, a figure which an annotation in this journal[1] regarded as so satisfying as to be described as a "residual core." It is now beginning to look as though, in the words of the boy eating an apple in the presence of a hungry and envious friend, "there ain't goin' to be no core." At least there will not be if all those concerned with maternity work take heed of the lessons to be drawn from this report. The Ministry of Health and the actively co-operating bodies—the Royal College of Obstetricians and Gynaecologists and the Society of Medical Officers of Health—are to be congratulated on the collection and publication of this material—material collected and published in such a way as not to hurt the feelings of any single member of the medical and nursing professions, and aimed solely to benefit the mothers of the future.

INSURANCE BENEFITS FOR B.M.A. MEMBERS

The Hospital Service Scheme approved by the Annual Representative Meeting at Torquay is the fourth special scheme introduced within the last two years exclusively for the benefit of B.M.A. members. To all who join before the age of 65 it offers on a world-wide basis and at a lower cost than any scheme previously available a full refund of all hospital or nursing-home in-patient charges within the maximum amount of benefit (£300 per annum) available to each person enrolled—that is to say, to the subscriber and his dependants. The scheme meets the main need of doctors who want private accommodation in nursing-home or clinic when ill. It also provides payments for various consultations, investigations, and treatments—including home nursing—and it allows for gifts to professional colleagues. Two unique features are that benefit is payable immediately upon enrolment, and those who join before the end of this year need not produce evidence of health either for themselves or for their dependants. This last concession will apply in future to new members who enrol within three months of joining the B.M.A.

Dr. I. M. Jones, when presenting this scheme to the Representative Body, made it plain that there was no intention of setting up a monopoly. There is nothing to prevent any group of doctors from joining the group schemes offered by other provident associations. These associations have played a valuable part in encouraging private independent practice in this country. The Council had hoped to utilize the services of all of them. But the Hospital Service Plan, organized by the London Association for Hospital Services, was the only one which met the Council's requirements that the scheme should be exclusive to B.M.A. members and should offer better terms than those offered to the general public. The Association has made a business arrangement on the best terms it could get with an organization which owes its beginnings to the medical profession and whose board of management, under the chairmanship of Sir Russell Brain, largely consists of representatives of the Royal Colleges and the B.M.A.

Another scheme recently introduced for B.M.A. members is the School Fees Plan. This has been arranged by the Medical Insurance Agency Ltd., in association with the Westminster Bank Ltd. (official bankers to the B.M.A.) and the General Life Assurance Company. It enables full members of the Association under the age of 50 who live in the United Kingdom, the Isle of Man, or the Channel Islands to spread the cost of educating their children over a long period at a reduced load. This is done by taking out an endowment assurance policy maturing in 15 years at a net annual outlay of between £100 and £110. After three years' premiums have been paid the member may borrow from the Westminster Bank up to £300 a year in each of the following seven years to cover educational expenses. During the seven years the only payments will be bank interest on the loan and the life-assurance premium. Ultimately the sum borrowed will be repaid by the maturity of the life policy, which also gives protection against premature death. Full details of this most valuable plan and its variations to meet individual needs and additional cover are clearly set out in a booklet[2] prepared by the Medical Insurance Agency.

The first scheme to be introduced, the Personal Accident Insurance Scheme, has been outstandingly

[1] *Supplement*, June 25, p. 390.
[2] British Medical Association School Fees Plan, Medical Insurance Agency, B.M.A. House, Tavistock Square, London, W.C.1.

successful, and 84,000 units have been taken up since it began two years ago. Because of its popularity it has been possible to extend it to provide at an exceptionally low cost weekly payments during periods of temporary total disability arising from accident. For an annual premium of 26s. members can qualify for £10 per week (maximum £30 per week) benefit for periods exceeding 14 days and continuing up to 52 weeks. The premium is increased by 6s. 4d. per unit for new entrants from the ages of 60 to 69, and participation ceases at the age of 70. This additional benefit, like the personal accident scheme of which it is a part, is available only to those normally resident in Great Britain, Northern Ireland, the Channel Islands, the Isle of Man, and the Republic of Ireland, but its cover is world-wide and includes accidents in private as well as in professional life. Yet another enterprise, launched by the Association last year to help young members, is the Young Practitioners Loan Scheme.

Dr. Jones and his Private Practice Committee are to be congratulated on their energy and resourcefulness in promoting these ways and means which bring such material advantages to members of the B.M.A. in such attractive terms. They are also one more proof of the debt the profession owes to the skilled services of the Medical Insurance Agency.

THE NIGHTINGALE TRADITION

One hundred years ago, on July 9, 1860, the first fifteen young ladies entered the Nightingale Training School at St. Thomas's Hospital to train as nurses. Celebrations are being held to mark the occasion. These include a centenary exhibition, which has been skilfully and attractively arranged at Doulton Hall, Lambeth, to show the development of the school and the part it has played in the growth of nursing as a profession, and the publication of an excellent account[1] of the school containing, among much else, letters from Florence Nightingale and many others. In addition Mrs. Lucy Seymer, herself a "Nightingale," has published a history[2] of the school which is a source of much interesting information. At the outset Miss Nightingale demanded financial independence for the nursing school, and the hospital was "reimbursed from the Nightingale Fund for the extra expenses to which the hospital is thereby put." The officers of the hospital also received remuneration "for their services in training probationers." The large sum of money collected as an acknowledgment to Miss Nightingale for her work in the Crimea formed the "Nightingale Fund."

Mrs. Seymer's book shows how great Florence Nightingale's influence has been, and still is, on the training of nurses. In her plan she had three basic principles—that the matron should have absolute authority over, and responsibility for, the nursing staff; that nurses should be trained for the work they were to do; and that while undergoing training nurses should live in a home which should be "a place of moral, religious, and practical training; a place of training of character, habits, intelligence; a place to acquire knowledge both technical and practical." It is of particular interest at this time, shortly after publication of the General Nursing Council's new regulations concerning a minimum standard of education for those wishing to train as nurses, to learn that in the Nightingale system there were two classes of probationers, the larger group being "nurse-probationers," who were "women of moderate education." They earned a small salary and received their training free. "Lady-probationers" formed the second and smaller group. They had received an education of a higher standard; they paid for their training and board and were not given a salary. The directors of new training schools were selected from this latter group, as also at a later date were all the ward sisters at St. Thomas's Hospital. Miss Nightingale held very firmly to the belief that "the key to the whole situation is the ward sister through whom the trained matron influences nurses, probationers, ward maids, and patients throughout the hospital." Therefore during training the future ward sisters were "more closely watched and criticized because more was demanded of them."

Some of the difficulties which arose in those early days are still problems to-day. One which is a constant subject for discussion at the present time is the teaching of the nurses in the wards. The pressure of work was apparently one of the reasons why this teaching was neglected, just as it is to-day. Miss Nightingale herself gave special attention to the preparation of nurses for senior posts, in particular administrative posts. Nearly a century later the nursing profession is only beginning to accept this special training as necessary. In one aspect only did Florence Nightingale fail to lead the way in the training of nurses. In 1895 the London Hospital introduced a preliminary training course during which probationers were prepared for nursing in hospital. It was not until 1910 that this was adopted by the Nightingale School. Florence Nightingale, as is very evident from Mrs. Seymer's book, was a woman with great foresight, great courage, and great opportunities, and she made full use of all three. In the hundred years of its existence the training school which she founded has made a contribution of inestimable value to nursing and thereby to medicine.

[1] *The Nightingale Training School, St. Thomas's Hospital, 1860-1960.* Privately printed for the Nightingale Training School for Nurses.
[2] Seymer, Lucy. *Florence Nightingale's Nurses: The Nightingale Training School, 1860-1960.* 1960. Pitman Medical Publishing Co. Ltd., London. Price 20s. net.

CANCER RESEARCH

The Scientific Report[1] presented last week at the annual meeting of the British Empire Cancer Campaign is a large volume containing accounts of many researches into cancer and problems relating to it. As in previous years the detailed reports from each centre are preceded by a summary, which this year occupies the first ten pages of the report. The compilation of this summary

must have entailed a great deal of work for the editors, because the reading and condensing of reports of scientific experts is a notoriously difficult task. This year it seems to have been done particularly well, especially in the section headed "Radiotherapy and Radiobiology," in which the sectional editor has succeeded in describing complex investigations in relatively simple language. Once again a useful feature of the summary is the bringing together of those reports from different centres which deal with similar subjects, thereby enabling comparisons to be made between the "results" being obtained by different workers.

The Scientific Report of the British Empire Cancer Campaign has become primarily a work of reference, and as such it is now indispensable to all research workers in cancer. A regular contributor to this report for many years was the late Professor E. S. Horning, a member of the staff of the Chester Beatty Research Institute, whose untimely death last November brought to a close a distinguished career. His many friends will naturally look to see what were his latest interests in the field of cancer research, and since his two contributions this year have a direct bearing on clinical medicine these have been chosen for brief comment here.

One of the surprises of experimental cancer research in recent years has been the induction of malignant tumours in rats, mice, and hamsters by the subcutaneous implantation of pieces of plastic. Horning had planned a thorough research into this phenomenon and had noticed that the tumours, usually spindle-cell sarcomas, arose from the connective tissue "pocket" laid down often within two months of implantation. He was particularly interested in the effect of stilboestrol on the development of these tumours, and found that when pellets of this substance were implanted with the "cellophane" films the incidence of tumours at the site of implantation of the film was reduced from 65% to 25% by the oestrogen.

Another research even more closely related to clinical medicine is the carcinogenicity of iron-dextran, a subject on which he had been working with Professor A. Haddow and which has recently been discussed in this journal.[2] Haddow and Horning first confirmed the discovery by H. G. Richmond of the carcinogenicity of the iron-dextran compound "imferon," and reported that the bulk of tumours appeared at the site of injection as sarcomas arising from the iron-laden connective and reticulo-endothelial tissues, but that tumours were found occasionally also in distant organs such as the liver and lung. It has since been found that the component dextran is by itself inactive, but Horning had planned further experiments to find out whether the potency of the complex is a function of the metal alone or of the entire complex. It is of additional interest that similar malignant tumours have also been obtained with aluminium-dextran. This research, in which Horning was so actively engaged at the time of his death, is now being continued both at the Chester Beatty Research Institute and at other centres.

[1] British Empire Cancer Campaign, *37th Annual Report*, part 2, 1960.
[2] *Brit. med. J.*, 1960, **1**, 788.

HYPERTENSION AND POLIOMYELITIS

Much has been written on the Continent about the development of systemic arterial hypertension during the acute phase of poliomyelitis, and this has recently been reviewed by a group of workers in Budapest, who have also made an extensive study of the association.[1] They investigated 336 children and adolescents, of whom 223 were admitted to hospital in 1957 with acute poliomyelitis and 113 were in hospital because of residual paralysis from an acute attack before 1957 (some as long ago as 1945). About a quarter of the patients in each group were regarded as hypertensive in the sense that their systolic pressures were 12 to 28% and their diastolic pressures 13 to 39% higher than the average normal for their age. A raised blood-pressure was four times commoner among those who had respiratory difficulty in the acute phase of the illness. It was also noted that the more extensive the paralysis the more likely was the development of hypertension. In the follow-up of the acute cases (during periods of 2 to 18 months) it was found that the hypertension persisted in about half of them. The cause of the hypertension remains obscure, though lesions of the diencephalon or autonomic nervous pathways have been suggested. In Great Britain the opportunity of studying this question may be small if the incidence of poliomyelitis continues to be as low as last year, but the Budapest authors make the interesting suggestion that E.C.H.O. and Coxsackie virus infections may have similar hypertensive sequelae. This point deserves to be followed up.

DR. H. GUY DAIN

When Dr. H. Guy Dain went to the microphone at Torquay to explain precisely the implications of a motion, the prolonged applause that greeted him made quite an inroad into the time available for him to speak. Everyone knew that within a few months of his 90th birthday he had decided not to seek re-election to the Council of the B.M.A. Dr. Dain's length of service of the Association must be unique in its long history. It is odd now to reflect that twenty-four years ago, at the Annual Meeting in 1936, he received the Gold Medal of the B.M.A. in recognition of his services, particularly in connexion with the administration of medical benefit under the National Insurance Acts. The award was made when Dr. Dain reached the age normally looked upon as the age of retirement. Yet what one might call his second innings for the B.M.A. called for even greater efforts and imposed even heavier responsibility on him. The prolonged ovation at Torquay showed how great is the regard and affection in which the present generation holds him. It is good to know that Dr. Dain has agreed to serve on one or two B.M.A. Committees, and that his practical and common-sense wisdom and long experience will still be put to use for the benefit of the Association with which his name has so long and so honourably been connected.

[1] Zimányi, I., Prohászka, M., Szondy, M., and Ormai, S., *Acta med. scand.*, 1959, **164**, 497.

MORAL ISSUES IN MEDICINE*

BY

THE RIGHT REV. R. C. MORTIMER, D.D.
Lord Bishop of Exeter

"Then He called His twelve disciples together, and gave them power and authority over all devils, and to cure diseases. And He sent them to preach the kingdom of God, and to heal the sick." (St. Luke ix, 1–2.)

The healing of disease has always been a recognized part of the work of the Church. As with the Saviour Himself, so with His followers, a part of their mission was to heal the sick. In the earliest days they did this by miracles. That is to say, by what we should call spiritual healing or faith healing. But it was not long before they turned also to medical science. The building of hospitals was a regular feature in the life of the early Church. In time spiritual healing gave way altogether to the application of medical science. The doctor took the place of the priest. Now it seems that there is a tendency to reverse the process.

The discoveries of psychology have led to a growing recognition of the influence of non-physical factors upon the physical body; that is to say, of the effect of mental and emotional disturbances upon physical and organic disorders. In medical circles I understand that the word psychosomatic is now scarcely ever off the lips of those who write and speak. Certainly it is true that there is an increasing collaboration between doctors and the clergy in the treatment of the sick. Physicians, surgeons, and psychiatrists alike are more willing than they were to call to their assistance the prayers and exhortations of the priest. And there is a far better understanding on both sides of the respective roles of medicine and religion.

For this we clergy are indeed grateful. And we are trying as best we can to make ourselves more efficient in dealing with the sick and to co-operate more intelligently with the medical profession. Medico-clerical discussion groups are springing up all over the country. We have in this diocese recently formed such a group with particular reference to the light thrown by modern psychological studies on the handling of pastoral problems. The initial membership was seventy and it is daily increasing.

But it is not of this that I wish particularly to speak to you this morning, but rather of certain moral issues which I find invariably crop up when there are discussions between clergy and doctors.

There are, I think, three main issues. They are "Should a doctor tell?"; euthanasia; and gerontology. There is also a fourth, abortion. But I do not intend to say much of that, because there is, I think, now general agreement between the medical profession and the Church about it.

Surgical Abortion

When the death of the foetus is incidental to the performance of an operation necessary to preserve the life of the mother, there is no argument but that the operation should be performed. Equally when the killing of a viable foetus is only a means to the preservation of a woman's health or reputation, there is, I think, general agreement in the medical profession with the view of the Church that such an action is not permissible. Nor is it permissible, in our judgment, when the baby is likely to be born maimed or in some way deformed. In such cases there is too much uncertainty for abortion to be held to be justifiable. We cannot say for certain that the baby will be maimed, and if, in fact, it turns out to be maimed, we cannot estimate the value of its maimed life.

Just as few would think it right to terminate a child's existence after it had survived for several months, however maimed or deformed it might be, so we hold it to be unjustifiable to kill a baby in the womb. Cases where the direct killing of the foetus is essential for the preservation of the mother's life are, I am told, becoming increasingly rare because of new surgical techniques. A doctor is rarely faced, I understand, with the agonizing dilemma that he may save either the mother or the child, but not both. But such a case does arise, I am informed, when the embryo is hydrocephalic and for one reason or another cannot be delivered by a caesarean operation. Here the embryo will in any case die in the course of labour, and its continued presence in the womb is a source of danger to the mother. To end its organic connexion with the mother's body, even though its death inevitably ensues, is justifiable as the only way of preserving the mother's life. The Church of Rome would dissent.

Chastity

There is also a fifth area of occasional disagreement. It arises over what I may call the indiscriminate use of contraceptives, and showed itself in the controversy which broke out over that unfortunate pamphlet published last year on preparation for marriage. Not that I personally thought that the pamphlet was nearly as bad as its critics made out. On the other hand, there is no doubt that the article on pre-marital chastity was unfortunately worded. I thought that I myself could have stated the arguments for and against pre-marital chastity more forcefully. But then I was never noted for modesty.

The Church, in loyalty to scripture, teaches and must teach the high value of pre-marital chastity. Yet I think the Church has been much to blame in taking too negative an attitude about this subject. She has, I think, been guilty of an exaggerated stress upon the shameful wickedness of fornication and on the deterrent value of the risks of venereal disease and of conception. She has said too little of the positive beauty of chastity, and of the loss of personal dignity and integrity which is involved in promiscuous sexual intercourse. She has said too little, also, of the positive value of chastity as a preparation for marriage itself.

The sexual act is a kind of sacramental channel for the expression and deepening of love between man and woman. It is cheapened and rendered less effective by its use as an expression either of lust or of a trivial and passing affection. But I do not propose to say more about that this morning. Because, for all that some psychiatrists are sometimes tempted to seek an easy way out in the cure or prevention of repressions and neuroses by encouraging sexual adventures, I think that

*Sermon preached on June 19 at the Official Religious Service in Upton Parish Church, Torquay, during the Annual Meeting of the B.M.A.

by and large throughout the medical profession there is general agreement that such advice raises more difficulties than it solves.

Telling the Patient

The problem of whether and when a doctor should tell his patient that he is suffering from an incurable disease is an intensely difficult one. And I think that the clergy, for the most part, recognize this—though some of course do not. On the one hand, many patients and their relatives do not wish to be told the truth. On the other hand, one can never be sure of that. And the maintenance of a relationship of complete trust and confidence between the patient and his doctor is of absolutely vital importance.

On the other hand again, in all cases of disease where there is the slightest chance of recovery, it is of the greatest importance to sustain and strengthen the patient's will to live and to surround him with an atmosphere of hope and courage. Nevertheless, it is the opinion of many of the clergy that by and large, and on the whole, doctors tend to conceal the truth to an unnecessary and unjustifiable extent. And by doing so they make the work of the clergy in preparing people to meet death unnecessarily difficult. We all have experience of persons who, knowing that they are under sentence of death, yet achieve a wonderful peace and serenity of mind as they prepare themselves for their end. But the decision to tell or not to tell is, I believe, the doctor's and it is often a very difficult one.

Euthanasia

From time to time the question is publicly ventilated whether doctors should be given authority to accelerate the death of those who are suffering from a painful and incurable disease. The Church has no doubt that euthanasia would, in fact, be murder; though there are some good Christians and churchmen who dissent.

I believe that doctors, for the most part, are extremely reluctant to have any such authority and dreadful responsibility thrust upon them. They believe that whether or not it is limited to the express request of the patient it would have a fatal effect upon the relationship of trust which now exists between patients and their doctors. They believe that it would gravely alter the whole *ethos* of hospitals, especially of those hospitals which care chiefly for the very old. I do not myself believe that in this country euthanasia is, in fact, a live issue. It is rather a matter of academic discussion.

In this respect it is very important to distinguish clearly between euthanasia itself on the one hand, and the administration of pain-relieving drugs in lethal quantities on the other. Whilst it is the duty of the doctor according to his Hippocratic oath to save life and not to destroy it, it is also his duty to use every possible means to alleviate pain. In performing this second duty it is often necessary for him to administer drugs in ever-increasing quantities. There is no doubt that in doing so he shortens the life of his patient and finally ends it. Nevertheless he does not fail in his duty and is not disloyal to his oath. For his object in thus administering the drugs is not the death of his patient, but the alleviation of his sufferings. This makes all the difference.

Striving to Maintain Life

The problem raised by gerontology, though not only by gerontology, is this. How far is it a doctor's duty to use every possible means to preserve that person's life? And, in particular, how far is it his duty in the case of a very old person?

It is, in general, the Christian view that while there is a moral obligation to maintain life by all ordinary means, there is no obligation to use extraordinary means. Ordinary means are such actions as do not cause grave hardship to the patient and which offer a reasonable hope of success. Extraordinary means are means which involve very great expense, inconvenience, or hardship and which at the same time offer no reasonable expectation either of success or of benefit.

In the case of the very old, whose faculties have failed or are failing, even ordinary means of preserving life have little hope of retarding the advance of senility; and their success in retarding death confers little benefit or happiness upon the patient. Nevertheless, since to deprive such patients of food and drink and simple medicines would be in effect to cause their death, such ordinary means of prolonging life must in all cases be employed. But there does not seem to be any moral obligation to employ extraordinary means in such cases.

To subject very old people to the acute discomfort of a serious operation or of feeding by intravenous drip would seem to be morally wrong. Such extraordinary means of preserving life should only be used where there is a reasonable hope of recovery from the disease and where some benefit or happiness is conferred upon the patient other than the mere prolongation of his bare existence. But when these conditions are present extraordinary means not only may but should be employed, as a moral duty. In other words, in this field of medicine there seems to be some truth in the old couplet: "Thou shalt not kill but needst not strive officiously to keep alive."

Christian Duty and Privilege

But I have wearied you for long enough with these moralizings. I will end with the text with which I began. I would remind you all of your sacred duty and high privilege to heal diseases. It is a sacred duty to the performance of which you must bring all the resources of modern science. For its performance you must continually re-equip yourselves with modern knowledge. According to your standing and calling in your profession it is your duty either to search for new discoveries and to forge new weapons against the last enemy, death, or with skilled knowledge and sensitive understanding to apply the discoveries of others to your patients.

But the healing of disease is not only your duty but your privilege. You are the inheritors of a Christian civilization. You heal diseases in the name of Christ and as part of the work which He has entrusted and commanded His Church to do. To you, as to His first apostles, He has given power and authority to cure diseases and has sent you forth in His name to do the works of His compassion. To Him, then, let us give the praise and glory for all the work which you do. For He, with God the Father and God the Holy Ghost, is the Lord of all life and health and to Him let us attribute all honour, power, might, majesty and dominion, henceforth and for ever. Amen.

British Medical Association

ANNUAL MEETING, TORQUAY, 1960

SUMMARY OF PROCEEDINGS

THE SECTIONS

SECOND SYMPOSIUM

Thursday, June 23

The Contribution of Medicine to Efficiency in Sport

After the President of the Association, Sir ARTHUR PORRITT (London), had briefly introduced the speakers, and had commented on the great importance of the subject, Sir ADOLPHE ABRAHAMS (London) spoke on "The Relation of Medicine to Sport—Yesterday, To-day, and To-morrow." The chief contribution of medicine had come from the laboratory rather than from clinical investigation, and the results, as well as being applied to sport, had been adopted by the physician in his practice. After early pioneer work on muscle contraction, chemistry, and circulation, the next study was of cardiac and respiratory rates, body temperatures, and blood-pressures after violent exertion. Transient proteinuria under such conditions, at one time viewed with alarm, was now regarded as of no significance; and the modern cardiologist held that the healthy heart could not be damaged by exertion. Diet was better understood, and instead of thinking that a high-protein, low-fluid diet was best (on the grounds that protein was strengthening and fluid weakening) it was now held that diet could be left to choice. Exercise was of much greater importance, and being a modern athlete was often a whole-time occupation. Training had to be continuous to get the best results.

Oxygen enhanced performance, but only if it was inhaled throughout. The optimum concentration was 30%, and the best results were obtained if the demand was kept steady so that the body became educated to work in a state of partial oxygen-want.

Of the future, Sir Adolphe thought that some wild predictions—for instance, a mile in 3 min. 47 sec.—were not possible feats; it was more likely that fractional improvements would come. But such statements had been made before, and events had discredited them. It was possible that biochemists might find some drug which would enhance the speed and force of muscular contraction, leading to new records.

Physiological Factors

Sir Adolphe was followed by Dr. R. G. BANNISTER (London), who talked about "Some Physiological Factors Limiting Athletic Performance." He said that physiologists were still puzzled as to how man ran at all, rather than how he ran at a particular speed. The main advances in athletic technique had come from athletes themselves, spurred on by competition. Body temperature was more difficult to keep down to a normal level in hot weather, and this was thought to mar athletic prowess. On the other hand, athletes spent some time before an event in "warming up." Experiments had been done to measure body temperature during sustained performance, and a steady rise was noted. If the experiment was carried out in hot weather, the athlete's temperature reached a level at which he broke down, and could not continue; in cooler air he could continue until other factors limited his efforts. It was likely that at the Olympic Games in Rome this summer the long-distance runners and walkers would suffer from this temperature effect.

Oxygen transport was another vital factor. Muscle contraction occurred under both aerobic and anaerobic conditions, the latter for a limited period, which was of use to sprinters, who could not absorb all the oxygen they needed during the time of a race. Capacity to use anaerobic muscular power was limited by innate qualities and could not be improved by training. Improvement in sprinting was gained by better starting and running techniques. In longer races, where aerobic mechanisms had to be used, oxygen transport was of great importance. Improved running skill, with the minimum expenditure of energy, reduced oxygen demand, and athletes also had greater diffusing capacity (power to absorb oxygen across the alveolar membrane) than normal subjects—hence their better results.

Marathon runners had other factors to contend with, such as falling blood-sugar levels, nervous fatigue, dehydration, and salt lack. The most important thing affecting any champion's performance was his competitive spirit. In many ways an athletic feat was like physical combat.

Biomechanical Studies

Mr. NORMAN CAPENER (Exeter) considered that medicine and sport had gained much from each other. It was important to understand how sports injuries occurred in order to try to prevent them. Fractures were easy to understand, but little was known about soft-tissue injuries. Mr. Capener showed some slides illustrating walking movements, and demonstrated how the up-and-down and side-to-side motions combine to carry the centre of gravity of the body forward along a spiral. This, together with the torsion stresses so often seen in sport, placed much strain on the lower back and pelvis. Too much had previously been made of static forces, and a new dynamic concept included the effects of motion, of braking actions, of paradoxical movements due to fixation of different parts while others were free to move, and the consequences of these. Some of Mr. Capener's illustrations showed the actions of flexors and extensors in the leg, illustrating how movement depended on how the leg was held or applied.

The part played by the subscapularis muscle in shoulder dislocations was explained. This was no lesion to be treated lightly by manipulation and "getting on with the game." Another illustration given was the meniscus injury caused by torsional stresses in the leg. The treatment was immediate removal from the field of play, reduction by manipulation, compression bandaging, limitation of flexion for some weeks, and physical measures to prevent loss of muscle tone.

Mr. Capener then illustrated some experiments which demonstrated the elasticity of bone and its great strength. Much of this depended on its protein content, and for bones to be equal to the stresses imposed on them by athletic performances it was important that the diet should have adequate protein content. Carbohydrates should be limited. Ligaments were particularly vulnerable to rotational and shearing forces, and serious damage to the cord in the cervical spine could occur with frightening ease when a rugger scrum collapsed.

Tennis elbow was possibly due to compression of the posterior interosseus nerve as it passed between the parts of the supinator brevis muscle and its aponeurosis. Mr. Capener had operated on six patients to relieve such pressure, and the results were satisfactory so far, but many more needed to be done to show whether this was the best treatment. It did encourage him, however, to suggest that more thought should be given to direct methods in other soft-tissue injuries. Much research was needed, and more doctors should take an interest in the special injuries of athletes.

The Athlete's Physique

Professor O. G. EDHOLM (London) amused his listeners by announcing that he had recently doubled Roger Bannister's record—that is, he had done a mile in eight minutes. He went on to show how athletes are peculiarly adapted to their particular sports, and illustrated his point with pictures of Channel swimmers. It was known that the usual survival time of adults in cold water was five hours, but these athletes lasted much longer than that. This was because they were covered well by fat, and smeared themselves with grease, so that they were insulated from the cold.

Incidentally, their total output of energy during a Channel swim was higher than for any other athletic feat.

Professor Edholm went on to explain how training affects performance differently in athletes and sedentary workers. His experimental subjects had mounted a 20-inch-high stool thirty times a minute until exhausted, and had repeated this feat daily. At first the sedentary workers could achieve only three minutes of this exercise, but after 30 days (one performance each day) they were able to continue for 15 minutes at a time. Athletes achieved 30 minutes in eight days, and stopped because they were bored rather than exhausted; their rate of improvement was much greater than that of the sedentary men. Subjects with previous athletic performance to their credit, but long ago, achieved a midway position. It followed that exercise, when pushed to exhaustion, left traces for at least 24 hours on which a superior performance could be built.

Another aspect of this was the recovery rate of the pulse after exercise. Here, again, the untrained subject developed greater tachycardia and took longer to recover than did the athlete; that is, the athlete's responses to the exercise were much quicker.

Some film loops showing weight-lifting and pole-vaulting were shown in slow motion. From these pictures Professor Edholm had measured speeds and distances, and with knowledge of the masses involved he had calculated work done. As much as 2.4 horse power was expended by the weight-lifter at one moment of his lift. The film loops were also of great interest to the performers themselves, and aided them to correct their faults. Physiologists and athletes had still much to learn from each other.

Miscellaneous Questions

In reply to members of the audience, Mr. CAPENER stated that deranged knees often settled down under the conservative regime he had advised, so that immediate operation was not wise. He thought that hydrocortisone reduced swelling in the tissues in cases of tennis elbow, which explained its therapeutic effect. He gave his opinion that boxing was health-promoting, but also dangerous. There was no reason he could see why the dangers should not be reduced by giving additional protection to the contestants, as had been done in fencing.

Sir ADOLPHE ABRAHAMS pronounced smoking to be deleterious to athletic performance, but it also had a sedative effect which might help an athlete to relax, and on balance it could be beneficial in some cases. Long-distance cyclists rarely smoked. He explained the absence of records in long-jumping as being due to a lack of interest in that sport: the best exponents were necessarily good sprinters, and preferred sprinting to jumping. Hypnotism and suggestion were valuable in so far as they induced a suitable state of mind, but they could not improve physical capacity. The best jumps were taken when the subject was being pursued by an angry bull.

Professor EDHOLM, answering a question on the effect of barometric pressure, said that performance was demonstrably poorer at 5,000 ft. altitude, and Sir ARTHUR PORRITT added that when games were held at 6,000 ft., the sprinters did better than the long-distance runners. This, as Dr. BANNISTER quickly pointed out, supported the aerobic–anaerobic muscle-contraction theory—sprinters did not need oxygen.

Questioned about adaptation to heat, Dr. Bannister replied that it seemed reasonable to attempt it, and Professor EDHOLM thought that acclimatization might be achieved artificially, but that deterioration would ultimately occur under hot conditions.

Sir ARTHUR scouted the myth that women should not indulge in athletics during menstruation or early pregnancy, which were both physiological states, and he concluded by pointing out that sport was a major industry; there was no country whose sportsmen were more respected than ours, and the discussion had been about a most important industrial disease.

SECTION OF PUBLIC HEALTH AND SOCIAL MEDICINE

Wednesday, June 22

Immunization Programmes

With the president, Dr. C. METCALFE BROWN (Manchester), in the chair, Dr. W. C. COCKBURN (London) presented the opening paper of a symposium on immunization programmes. He assumed that there was general agreement that immunization against smallpox, diphtheria, pertussis, poliomyelitis, and tetanus should be carried out on a community scale, and summarized the problems to be surveyed in the rhyme "Early or late? Mixed or straight?"

Referring first to the psychological impact of repeated injections in early childhood he doubted whether much could be deduced from the more complacent reaction of the very young child to jabs and the rather more vociferous response of the slightly older child. Immunization too early in life could produce a poor protective response, as some maternal antibodies might still be circulating and the antibody-producing mechanism might not be fully functioning. The present poliomyelitis vaccines did not produce an adequate response before the seventh month of life.

Immunization procedures must be arranged to protect the child before he was likely to be exposed to the specific infection. With diphtheria, poliomyelitis, and tetanus this hardly arose before the age of 1, but with pertussis over 9% of the cases and as many as 69% of the deaths occurred during the first year of life. Even here, however, there had been a tremendous reduction over the last decade; the number of cases had dropped from well over 100,000 to about 33,000 and deaths had fallen from about 400 to 25 annually: 52% of these deaths occurred before the age of 6 months and in many of them infection must have occurred soon after birth—that is, even before early immunization could have been effective. It might therefore be rational to immunize towards the end of the first year and to try to ensure the young infant's protection against whooping-cough by comprehensive immunization of the slightly older child, who would then no longer be a source of infection.

Mixed Antigens

On the choice between single and mixed antigens, Dr. Cockburn said that the findings of a Medical Research Council committee published in 1956 appeared to be supported by preliminary results of a more recent survey of cases of "provocation" poliomyelitis. There was a significant difference between the risk from single and from combined (diphtheria/pertussis) or triple (diphtheria/pertussis/tetanus) antigens. It was true that this risk was small, but it was children who were fit and well who were being immunized and therefore only the very safest methods should be used. One way to ensure this was by the use of single antigens, but this entailed a large number of injections. The obvious alternative was to immunize children first against poliomyelitis and then against the other conditions. Dr. Cockburn advocated a primary course of poliomyelitis vaccination at 8 or 9 months, followed by three doses of the triple antigens and by a booster dose of poliomyelitis vaccine at 18 months of age. Smallpox vaccination could be carried out at 7 months or at any other time during the first 2 or 3 years of life. A further dose of triple antigen should be given at school entry, a dose of diphtheria and tetanus toxoid at 8 or 9 years, and finally B.C.G. at about 10 or 11.

Immunization Schedule

Dr. IAN TAYLOR (London) stressed the advantage of combined prophylactics which reduced the number of defaulters during the programme. So far as the risk of provocation paralysis was concerned, 180,000 injections with combined and triple prophylactics had been given in London in 1958 and 1959 and only one case of paralysis of the injected limb had occurred within 28 days, an incidence of paralysis about one-tenth of that reported in the Medical Research Council report.

Active immunization against tetanus was far safer than passive protection; nearly a million doses of antitoxin were being given each year with some thousands of attacks of serum sickness and 16 deaths between 1945 and 1957. Injections of tetanus antitoxin could sensitize the patient, with the result that antitoxin given subsequently was too rapidly secreted. Many fatal cases of tetanus were the result of wounds which had not been considered sufficiently serious for prophylactic antitoxin.

When planning an immunization programme one must have in mind that poliomyelitis vaccine did not exert its maximum effect until after the age of 7 months. In order to reduce the mortality from pertussis still further this vaccine had to be given early. If diphtheria immunization was given in the first three months of life the response might be inadequate in some children; a reinforcing dose was therefore required at 15 to 18 months. On the basis of these facts "Immunization Schedule B" recommended in the Wellcome Symposium of 1959 (see report in *B.M.J.*, May 23, 1959, p. 1342) was now in operation in London. Three injections of triple antigen were given from 2 to 4 months, followed by smallpox vaccination at 5 months, and two doses of poliomyelitis vaccine at 7 to 8 months. At 15 to 18 months one further triple and one booster polio injection were given, and at school entry a further booster with combined diphtheria/tetanus antigen. This scheme was already proving acceptable to staff and parents alike. It required some adjustment for children in whom immunization had to be started later; after the age of 5 or 6 months the urgency of whooping-cough immunization became less and that of protection against poliomyelitis greater, and the course of poliomyelitis injections was therefore given first.

The occurrence of cases of diphtheria among school-children in three different areas in London during the last two years had underlined the great importance of maintaining immunity to diphtheria during school life. As long as a reinforcing dose was given at 15 to 18 months and a booster at school entry there was probably no need for further booster doses during school life.

A personal record, especially of tetanus immunization, was obviously essential. In London a card had recently been introduced whose function was not only to record the immunizations but also to assist the doctor or health visitor when discussing the infant's immunization programme with the mother and to act as an appointment card.

Consumer Interest

Dr. E. HUGHES (Reading) stressed the value of the personal advice given to mothers by doctors and health visitors in the propagation of immunization programmes. Such programmes must be based primarily on the optimum protective result, but also on convenience to the patient, and lastly on the ease with which they could be administered. In Reading, too, Schedule B had been adopted, with smallpox vaccination very early in life. He had been disturbed by the recommendations of the Medical Research Council committee, and it was interesting to speculate whether these recommendations might not now be modified in view of the lower prevalence of poliomyelitis in the community. Consumer interest must be considered; at the present time immunization against diphtheria alone would have a very small sale. The parents of to-day were no longer afraid of diphtheria, but they knew whooping-cough and they knew lockjaw.

Programmes should be regularly reviewed, and the time might soon come when routine B.C.G. immunization of school-leavers was no longer justified. A new situation would arise if a quadruple antigen were made available. How rational were our present programmes? Now that the likelihood of subclinical infection with *C. diphtheriae* in adolescent and adult life had disappeared, should not booster doses be repeated regularly throughout life?

Discussion

Dr. H. J. PARISH (Beckenham, Kent), who opened the discussion, took up the question of the psychological effect of immunization programmes. The complacent attitude of the young baby had an important psychological effect on the mother, who was much more likely to bring him back for further immunizations. At a recent international conference 10 out of 11 countries had reported that they gave triple antigen early in life. The risks discussed in the Medical Research Council report had been overstressed, and he supported immunization with triple antigen as soon as possible after the first month of life.

Dr. Parish welcomed the introduction of record cards. The suggestion to record immunization by tattooing carried with it the risk of homologous serum hepatitis. Personally, he favoured engraved metal disks rather like the identity disks carried by members of the Services.

Surgeon Captain E. JAMES (Plymouth) asked what method of sterilization of needles and syringes should be adopted when a central syringe service was not available. The speakers agreed that, provided that boiling was done adequately and syringes and needles were kept sterile afterwards, this should be entirely safe.

Dr. LORNA M. ROZNER (South Shields) asked about the maximum intervals between injections of the triple antigen.

Dr. COCKBURN replied that it was difficult to give a definite answer, but in his opinion intervals of two months between the first and second and of four months between the second and third should not be exceeded.

Dr. E. D. IRVINE (Exeter) supported early immunization and the use of triple antigens. Immunization programmes must not be changed too often if the confidence of the public was not to be undermined.

Dr. AVIS M. BLUNDELL JONES (Exeter) suggested that active immunization against tetanus of children now attending school should be pursued on a national basis. She had had an excellent response from parents of girls attending two Exeter schools, and the casualty officers at the local hospitals, whom it was essential to put in the picture, had expressed interest and support.

Dr. J. S. G. BURNETT (Preston) considered it more rational to commence inoculation after the age of 6 months, when the likelihood of success was greater. In his area pertussis hardly ever occurred in children under 1. He had not introduced tetanus immunization and saw no necessity to do so now when the morbidity and mortality from tetanus was decreasing. Did not the main risk of tetanus occur in middle life, and how was this affected by protecting infants and young children?

Dr. COCKBURN estimated that there were still some 200 cases of tetanus every year and that 750,000 doses of A.T.S. were given annually. If a primary course of two injections followed by a third a year or so later and two or even only one boosters were given the risk of death was extremely remote, especially if a reinforcing dose was given after the injury. Dr. TAYLOR commented that as passive immunization was carried out so universally after injuries it was logical to introduce active immunization, which was so much safer.

Dr. K. O. A. VICKERY (Eastbourne) called for a nationally agreed programme. Having in mind the frequent movements within the population the present position was chaotic.

SECTION OF CHILD HEALTH

Thursday, June 23

Pneumonia in Childhood

Dr. VICTORIA SMALLPEICE (Oxford), the chairman and a vice-president of the Section, opened a discussion on pneumonia in childhood by reminding her audience that pneumonia still remained a killing disease and was responsible for much chronic respiratory infection. Dr. BERYL D. CORNER (Bristol) provided a fresh classification of pneumonia, as the old anatomico-pathological divisions did not allow for the influence of age, the variety of infectious agents, or various predisposing causes such as aspiration, malnutrition, muco-viscidosis, and asthma. Hospital organisms were carried home by the 70–80% of babies who were born in hospital,

and the incidence of different pathogenic organisms had been altered by antibiotics.

Dr. C. W. MARSHALL (Exeter) said that it was difficult for a general practitioner to think in terms of pathological classification: on an average he would have only 30–40 children in each yearly age-group in his practice, and he would have to treat each case individually. In Exeter during 1926–8 there were 55 deaths notified as due to pneumonia, 30 of them in infants less than 1 year old; in 1957–9 there were only 2, both in infants. In the intervening period there had been two startling changes—improved nutrition in working-class families and the development of ability to knock out infections at the start.

Dr. H. R. JOLLY (Plymouth) discussed the diagnosis of pneumonia in children: it was still a bedside matter of appreciating alterations in breathing, restlessness caused by anoxia, retraction of the head and bulging of the eyes in a dyspnoeic baby, and so on. A stethoscope was a hindrance, for it encouraged one to wait for the appearance of late signs before making a diagnosis.

Virus Pneumonias

Dr. B. E. ANDREWS (Manchester) said that 10 years ago there were few viruses known to cause pneumonia, but now there were about 50. Only the influenza and adenoviruses were really well documented as causes of pneumonia, though many others occasionally acted in this way. The adenoviruses might be responsible for 10% of cases, the virus could be recovered and there was a specific histological picture. Probably 20–30% of hospital cases were viral infections.

The panel answered many questions asked by members of the audience. The use of radiology for diagnosis was deprecated: its value lay in detecting persistent collapse after clinical recovery. Bacteriology should not be allowed to delay immediate treatment, but the results turned up helpfully when the first therapy was found to be ineffective. Virological investigation was useless unless started early—within 48 hours for recovery of adenovirus or within seven days for serology. The advisability of admission to hospital depended on such things as the degree of apparent toxaemia, how close a touch the practitioner could maintain, the competence of the mother ("Give her the benefit of the doubt"), and age. All young infants with pneumonia who showed respiratory distress should go to hospital, including those who had whooping-cough.

Heart Disease in the First Year of Life

The president, Professor A. V. NEALE (Bristol), took the chair at a symposium on heart disease in infancy. After quoting Blake's lines:

> "Art and science can not exist
> But in minutely organized particulars"

Dr. JOHN APLEY (Bristol) discussed the minute particulars of physical examination in babies with malformed hearts. In "cold" diagnosis the use of one's eyes, hands, and ears would go a long way, he said, although ancillary methods would almost always be needed too. Five important questions made up a cardiac catechism: Was there evidence of organic heart disease? Was it congenital or acquired? Was there obstruction or a shunt? Was the shunt from right to left or vice versa? Where was the lesion?

Dr. Apley showed how the unaided senses could provide the answers, but it was not enough just to observe the abnormal particulars; they had to be organized so that a working model of the patient's heart was built up in the mind's eye. What he called "hot" diagnosis was the diagnosis of heart failure, which was often unsuspected because its manifestations were different in adults and in infants. This diagnosis was essentially a bedside matter; the clinical findings were all-important, while ancillary methods were at that stage unhelpful and could be dangerous. Dr. Apley's contribution included the showing of what must be one of the shortest medical films ever exhibited, an effective demonstration of the detection of hypertrophy of the right ventricle by abdominal palpation.

Higher Mortality

Dr. IAN M. ANDERSON (London) discussed the high mortality due to congenital heart disease in the first year of life; it might be 70% overall; in his own series of 134 cases 64 died from a wide variety of abnormal conditions. In 100 cases angiocardiography, cardiac catheterization, or dye-dilution studies were done. Investigation was a contributory cause of death in eight cases, but in only two was the condition remediable by surgery. The total mortality rate was much higher in 34 patients not specially investigated than in the main group. Dye-dilution curves had not been helpful, but the other investigations gave correct and complete diagnosis in 38 of the 68 who had been followed up to operation or necropsy, while in a further 11 the main abnormality was detected although the diagnosis had not been correct in all respects.

Dr. Anderson showed on the screen a series of examples of his findings. So also did Dr. F. G. M. Ross (Bristol), who indicated the value of the simpler radiographic procedures—plain photography and screening with and without barium swallow. He emphasized, as Dr. Apley had also done, the necessity for good judgment in deciding when the more complicated techniques were necessary and demonstrated particular abnormalities revealed in each case by the most apt radiological method.

Complex Abnormalities

Professor A. L. D'ABREU (Birmingham) had studied the abnormalities discovered *post mortem* in infants with congenital heart disease. Their complexity was discouraging, but although it could not be ignored, it must not prevent the thoracic surgeon from looking for the little bits he could put right. His first choice would be patent ductus arteriosus, which was still often missed in the first three months, but which was a considerable cause of death. In 35 cases in which operation was done in Birmingham during the first year there had been three deaths.

The surgeon's second choice would be coarctation of the aorta. Simply that, not further identified in any complicated classification, but needing treatment because on the whole coarctation caused death during the first three months. In 13 cases in this age-group operation had been followed by death in four. In five there was also a ventricular septal defect, but in two of them the defect seemed to have disappeared when a cine-angiocardiogram was taken after operation. One important, but little-noticed, effect of operation was that children did not get out of breath so easily afterwards, and indeed the pulmonary wedge pressure was found to fall after operation.

The treatment of cyanotic heart disease at this age was disappointing; transposition of the great vessels was an unsolved problem, and open cardiac surgery was unsuccessful in cases of Fallot's tetralogy; the pulmonary vascular tree seemed not to have grown enough. Shunt operations such as Potts's anastomosis of aorta and pulmonary artery gave good immediate results but were difficult to undo when complete correction was attempted later. In Birmingham they had been putting a graft from the aorta to the pulmonary artery of the left lower lobe, which was well away from the site of further operation.

Dr. NEVILLE R. BUTLER (Swindon) analysed figures, from the Perinatal Mortality Survey, of deaths due to congenital heart disease occurring in the first month. Numerous though they were, the nature of the various anomalies of the heart and other organs offered little hope for surgery in this early group. In conclusion, the PRESIDENT emphasized the importance of three things of which time had not permitted discussion: early nursing care; prevention of respiratory infections, which caused a breakdown in a previously stable situation; and the prompt treatment of acute heart failure.

Dawson Williams Memorial Lecture

The Section met again after the symposium to hear Dr. W. W. PAYNE deliver the Dawson Williams Memorial Lecture on the subject of "Hypoglycaemia."

SECTIONS OF CHILD HEALTH, GENERAL PRACTICE, AND PSYCHIATRY

Friday, June 24

Role of the Family Doctor in Child Psychiatry

Dr. A. P. NORMAN (London) was in the chair at this discussion on the part which the family doctor could play in the prevention and treatment of neurosis in children. Dr. GERALD GARMANY (London) saw in his clinic no disorders related to the 11-plus examinations, although most of his patients were of school age. Over two-thirds were referred by general practitioners or by paediatric consultants. He regretted that, in London, school doctors were not permitted to send children to his clinic but had to refer them to a "problem cases conference." It was not as easy to write confidentially about a patient to a conference as to an individual with medical or nursing training. According to the Ministry of Education "child guidance is synonymous with education itself." If the term had thus lost its special meaning it should be abandoned, for the psychiatry of childhood was a part of medicine, not education. A comprehensive child-guidance service was being planned: education authorities were more ready than hospital boards to provide facilities, and before long the service might be taken away from the hospitals where it belonged.

Dr. Garmany discussed aetiological factors, which in his group were virtually all located in the child's home. He believed that there was great scope for collaboration with local-health-authority clinics in preventing illness of emotional origin.

Finding Time to Listen

Dr. ROBERT F. BARBOUR (Bristol) said that the family doctor was in a good position to see the stresses within a family and to help the children. There was, however, some danger that he might just inculcate his own beliefs, because that was more comforting to him than trying to find out what was best. Symptoms should be understood in their setting: nonconformity could show itself, at different ages, in refusal to use the pot, resistance to going to bed, truancy, or sexual misdemeanour. The concept of misplaced aggression explained much; if the wife was disappointed in her husband she might take it out on the child; if the school was repressive the child might rebel at home.

The instruments in the doctor's bag should include reading tests and some simple form of intelligence test. It was difficult to get a child's confidence—and difficult for a family doctor to be able to find time to listen unhurriedly and without interruption.

Rearrangement of the Medical Syllabus

Dr. J. P. M. TIZARD (London) discussed ways in which general practitioners might deal with specialist problems, and concluded that the students' syllabus would need to be rearranged. All students might, for example, have two years' basic medical education; some should go on to train for hospital work and others for general practice. These would need special teaching in their main subjects: emergencies, "minor medicine," and psychiatry. Child guidance, *pace* Dr. Garmany, did not primarily belong in hospital. In practice the family doctor would not need to know much about specific psychoses but he would have to understand illnesses like asthma, and in this field psycho-analysis had much to offer. It would be objected that a medical student had no time for a training analysis, but five hours a week for four years was not enormous in a course taking 40 hours a week for six years. A family doctor was bound to be in part a psychiatrist, but need not always be, as he is now, one who has trained himself, nor would he replace the specialist psychiatrist, who would still be needed.

Inadequate Facilities

According to Dr. G. H. SMERDON (Liskeard) the family doctor acting as psychiatrist did not need the puppets and paints: he was in the picture himself. He saw his patients in the unorganized phase of their illnesses, when prevention was better and cure easier. Only 5% of the children in his practice were emotionally disturbed, and these came from families with a high rate of psychological abnormalities. Many apparently normal children coped well with severely disturbed parents. Facilities for the treatment of neurosis were inadequate, and unless the family doctor responded to this challenge the gap would be filled in other ways, as it had been in the sorry story of antenatal clinics. Analytically oriented group psychotherapy would facilitate a limited, though distinct, change in the student's or doctor's personality. Thus fortified, the family doctor could become a good psychotherapist and could free specialist psychiatrists to be consultants.

Dr. H. S. PASMORE (London) cited a paediatrician who used a psychiatric social worker. What an indictment of the general practitioner. He was the person to treat common emotional disorders, and he should have access to the psychiatric social worker as he had to *x* rays and pathology. The practitioner should be trained to see the patient as a whole, not as an assembly of parts, and he should measure up to the new demands made on him by the increasing complexity of life and the greater number of disturbed children. Medical students in some schools were beginning to be taught in ways which fitted them for practice; the practitioner could be trained to do limited psychotherapy without himself having a formal analysis. Dr. Pasmore attended weekly seminars to which some of the other doctors found it worth travelling over 100 miles. The root of neurosis lay in the anxiety of childhood. One had to listen to parents and to get them to understand why the child behaved as he did.

In subsequent discussion Dr. E. B. STRAUSS (London) deprecated the uncritical use of psycho-analysis for training medical students. Dr. LINDSEY W. BATTEN (London) thought that doctors with huge lists would have difficulty in finding time to listen. Dr. BERYL D. CORNER (Bristol) said that a general practitioner would not need a psychiatric social worker, since he already knew the background of the case, and Dr. HUGH R. JOLLY (Plymouth) felt that if the family doctor had time and was conscientious there would be no need for a paediatrician to have one attached to him either.

SECTIONS OF ORTHOPAEDIC SURGERY AND RHEUMATOLOGY

Thursday, June 23

Treatment of Osteoarthritis

The president of the Section of Rheumatology, Dr. W. S. C. COPEMAN (London), was in the chair. Mr. NORMAN CAPENER (Exeter), president of the Section of Orthopaedic Surgery, joined the other members of the panel, Mr. H. OSMOND-CLARKE (London), Mr. W. D. COLTART (London), Professor J. H. KELLGREN (Manchester), and Dr. R. M. MASON (London).

Five main questions were discussed by the panel. The first was: How would the panel assess the prognosis of osteoarthritis of the hip? Professor KELLGREN emphasized that there were two distinct types of osteoarthritis. The polyarticular variety with several joints affected, and with Heberden node formation, carried a much better prognosis than the type in which the hips alone were chiefly involved. Dr. MASON pointed out that it was sometimes difficult to put a patient into one of these two separate groups. Mr.

COLTART added that osteoarthritis usually carried a worse prognosis in the hip than in other joints.

The second question was: What is the operation of choice for osteoarthritis of the hip? Mr. CAPENER regretted that at present there was no ideal operation. The requirements of such an operation were the cure of pain and deformity, and at the same time the restoration of full stability and movement. Intertrochanteric osteotomy was a sound and safe procedure. Mr. OSMOND-CLARKE endorsed the value of osteotomy for unilateral cases, but felt that cup arthroplasty was probably the operation of choice when both hips were involved. Dr. MASON expressed doubt about the late results of prosthetic arthroplasty, but the meeting was most fortunate in having Dr. AUSTIN T. MOORE (Columbia, South Carolina) in the audience. Dr. Moore had followed 92 cases for over ten years after his arthroplasty operation, and the results had been most satisfactory. Accurate pre-operative assessment of the patient, an experienced surgeon, and careful post-operative treatment were all necessary to produce a successful result.

The third question, "How should corticosteroids be used in the treatment of osteoarthritis?" produced a unanimous opinion that the use of corticosteroids by mouth in the treatment of osteoarthritis should be condemned. The surgical member further stressed the dangers of operating on patients who had taken corticosteroids even two years earlier. They made a plea that general practitioners should inform surgeons when their patients had taken these drugs. Local injections of hydrocortisone into joints were often beneficial. Mr. CAPENER emphasized the need for strict asepsis whenever these injections were given.

The fourth question was: What do the panel think is the place of osteopathy in the treatment of osteoarthritis of the spine? It was agreed unanimously that osteopathy had no place in treatment of this disorder, but most members considered that a judicious manipulation performed at the right time was a very good procedure.

The panel, answering the fifth question—Is physiotherapy simply an expensive form of placebo in the treatment of osteoarthritis?—generally agreed that properly planned physiotherapy had a very definite place in treatment, and the CHAIRMAN stressed that there were definite principles of treatment to be observed. Mr. COLTART drew attention to the risk of physiotherapists being asked to devote time to patients unlikely to derive benefit from treatment at the "expense" of those who would do so.

SECTION OF ORTHOPAEDIC SURGERY

Thursday, June 23

Hallux Valgus

With the president, Mr. NORMAN CAPENER (Exeter), in the chair, Mr. G. N. GOLDEN (Guildford) read a short paper on the osteotomy operation for hallux valgus. Palliative operations for hallux valgus, such as removal of the exostosis, had frequently been followed by a recurrence of symptoms after five to ten years. Arthrodesis of the metatarsophalangeal joint and various types of arthroplasty impaired the overall efficiency of the foot. Mr. Golden therefore preferred, particularly in young people, an operation which corrected the varus deformity of the first metatarsal by a wedge osteotomy at its base. In making this osteotomy a small spur was fashioned on the lateral side of the metatarsal base in order to prevent subsequent displacement of the shaft. The soft tissues on the lateral side of the metatarsophalangeal joint were divided, and the bursal flap on the inner side sutured under tension. The foot was immobilized in plaster until six weeks after the operation.

The results of 149 operations in 85 patients were given between two and ten years after operation. 78% of the patients were free from pain, and a further 16% had only slight pain and no disability. Objectively it was found that 60% developed less than 10 degrees of valgus after operation. 87% had over 45 degrees of movement in the metatarsophalangeal joint. Mr. Golden stressed that a successful result depended on adequate correction of the metatarsus primus varus.

In the ensuing discussion Mr. G. BLUNDELL JONES (Exeter) mentioned the relapse of the varus deformity of the first metatarsal after initial correction by other varieties of osteotomy. Several speakers agreed on the inadequacy of a screw holding the first and second metatarsal bones together.

Reticulum-cell Sarcoma of Bone

Mr. D. LLOYD GRIFFITHS (Manchester) stated that most people now accepted the fact that a primary reticulum-cell sarcoma of bone did exist, though some made the diagnosis too readily. The greatest difficulties lay in distinguishing primary reticulum-cell sarcoma from generalized reticuloses clinically simulating isolated osseous lesions, from metastasis of undifferentiated tumours, and from osteomyelitis, notably the latter. Of 37 cases submitted either to the Manchester University Department of Osteopathology or to the Manchester Royal Infirmary in the last 22 years the diagnosis had been upheld with certainty in only 14. In these cases the clinical history and behaviour of the tumour had been considered with a double-blind check of the histology. It was desirable to be prepared to admit doubt regarding the diagnosis, and if necessary to defer a definite decision for perhaps five or six years.

Microscopically the tumour, apparently originating in the medulla, produced a large, soft, friable mass round the bone, which was eroded. Histologically the appearances were similar to those of reticulum-cell sarcomata which originated in other tissues. The cells were poorly defined and had abundant cytoplasm. They had a syncytial appearance and did not lie in any definite pattern or formation. The *x*-ray appearances of the tumour were not characteristic and often resembled those of secondary carcinoma. Occasionally in the early stages a little subperiosteal new-bone formation had been noted.

As to treatment, Mr. Lloyd Griffiths advised resection of the tumour where possible, pointing out that long survival was likely in more than 50% of cases. The longest survival in this series had been 23 years.

Mr. H. OSMOND-CLARKE (London) agreed that pathologists alone were unable to give a definite diagnosis, which could be reached only after knowing the ultimate behaviour of the tumour.

Surgery in Ankylosing Spondylitis

Mr. W. ALEXANDER LAW (London) first considered the temporo-mandibular joints. If these had become fused, resection of the condyle on one or both sides enabled the patient to talk and eat more easily. It also facilitated the task of the anaesthetist should any further surgery be considered. No prosthesis had been found necessary in these joints.

Mr. Law described the operation of spinal osteotomy to correct rigid kyphosis. The purposes of the operation were (*a*) the correction of severe deformity to improve appearance and visual range, and (*b*) the relief of the pressure of the costal margin on the upper abdomen, thus improving respiratory and gastro-intestinal function. In cases with severe deformities correction by stages was sometimes needed, though in the lower lumbar region as much as 90 degrees correction in one stage had been achieved and maintained without neurological involvement. The results of spinal osteotomy performed during the last 13 years in over 100 cases were given. Six deaths had occurred in the early post-operative periods; three of these were considered to have been caused by previous corticosteroid therapy.

Five cases of osteotomy in the cervical spine had been performed. It was possible to achieve 20 degrees correction in a single stage. There had been one death, probably due to earlier steroid therapy. For involvement of the hip-joints

cup arthroplasty or pseudo-arthrosis operations had been performed in 36 patients two to thirteen years ago. Surgical revision of a mould arthroplasty had sometimes been necessary even two or three times. Unilateral cases gave better results than bilateral. Arthroplasty operations on the knee using a Shiers hinge had only given a very limited success because of the liability to fibrous, or even bony, re-ankylosis.

In the ensuing discussion Mr. LLOYD GRIFFITHS drew attention to the not-infrequent occurrence of fractures of the cervical spine in patients with ankylosing spondylitis.

Primary Treatment of Open Injuries of the Thumb

Mr. R. H. C. ROBINS (Exeter) reminded his audience that vascularity was the key to the preservation of injured tissues. The object of treatment was to steer a middle course between wanton destruction of useful remnants and over-optimism in preserving dead structures. More could often be achieved at the initial operation than could be retrieved later. In an incised wound which was satisfactory an immediate tendon or nerve suture could be performed primarily. Suture of flexor pollicis longus gave a better prognosis than of the deep flexors of the fingers, and a failed primary suture in the thumb did not prejudice the result of a free graft later. With more extensive injuries in which everything had been divided except one neurovascular bundle it was necessary to stabilize the thumb by a Kirschner wire fixation of the bone. This method was the safest and simplest method of dealing with the instability of severe crush injuries and compound fractures.

Severe injuries at the base of the thumb sometimes left the distal parts undamaged. Wire stabilization of these injuries was preferred, and while maximal length was important no attempt was made to prolong this at the expense of vascularity. In cases of partial amputation of the thumb, skin defects could often be better repaired by free grafts or flaps rather than amputating more proximally. Sometimes a skin flap could be taken from a mutilated index finger. If the thumb had been avulsed near the base of the proximal phalanx, leaving bone projecting through an area of circumferential skin loss, it was often necessary to apply a small tubed pedicle from the opposite arm. The tactile surface of the thumb was covered with sensitive skin by advancing distally the skin from the thenar eminence. A thumb made larger, but devoid of sensation, had little or no value.

Mr. R. G. PULVERTAFT (Derby) emphasized the value of internal fixation of unstable thumb injuries. Mr. H. OSMOND-CLARKE (London) told the meeting of the surprisingly good function he had seen in hands from which the thumb had been lost several years.

Dupuytren's Contracture

Mr. IAN W. WINCHESTER (London) discussed the pathogenesis of Dupuytren's contracture, mentioning an older theory that the condition was the result of diffuse benign fibrous hyperplasia leading to scar formation. More recently Vernon Luck had suggested that the essential lesion was the nodule. This nodule underwent proliferative cellular hyperplasia, and later the fibroblasts became arranged in ordered lines. Still later the nodule contracted and went through an involution phase to become almost acellular.

Total excision of the palmar fascia had been advised in the past as the best treatment, and this had been based on the old ideas of pathogenesis. Mr. Winchester had carried out less radical operations, removing only the nodules and diseased fascia. Furthermore, it was possible to predict from the position of the nodules whether contracture would occur. The operation had been performed on 30 patients and its technique was well shown on a film.

In the ensuing discussion Mr. C. C. JEFFREY (Exeter) inquired about cases in which the contracture recurred many times after several operations. Mr. R. G. PULVERTAFT (Derby) considered that these patients, most of whom were young adults, constituted a very definite group.

After thanking the speakers for their excellent papers, the PRESIDENT expressed regret that the audience was composed almost entirely of orthopaedic surgeons. The papers had been on subjects of wide interest both to general practitioners and to those working in other specialties, and it was a pity that the meeting had not been more representative.

Friday, June 24

Clinical Meeting

By invitation of the president (Mr. NORMAN CAPENER) and the hospital staff a most interesting clinical meeting was held at the Princess Elizabeth Orthopaedic Hospital, Exeter.

Mr. F. C. DURBIN presented three particularly difficult cases of osteoarthritis of the hip undergoing treatment in the hospital at that time. He also showed a child with redislocation after conservative treatment of congenital dislocation of the hips; the problems of management of some of these cases were discussed. A case of slipped upper femoral epiphysis was presented, and also an elderly patient who had had an Austin–Moore prosthesis inserted after non-union of a subcapital fracture. Mr. Durbin found this prosthesis invaluable in a salvage procedure when faced with non-union, but did not recommend using it as an alternative to nailing when dealing with recent fractures.

Mr. G. BLUNDELL JONES presented three children undergoing treatment in the hospital for Perthes's disease. He confessed to being perplexed about the best management of children with this condition, having followed up cases in which bed-rest with traction had been started before the appearance of radiological changes. These children had been admitted to hospital with "observation hips." Despite the institution of complete rest early in the disease, the end-results had been no better in these cases than in the others. In view of this it was suggested that perhaps one was not justified in admitting children with Perthes's disease to hospital for prolonged rest. The value of out-patient treatment by means of a sling, or a weight-relieving calliper, was also considered to be very doubtful.

Mr. C. C. JEFFERY presented a patient who had sustained a severe de-gloving injury of the wrist, hand, and proximal parts of the fingers. At operation the subcutaneous tissue had been removed from the flap, which had then been sutured back into position, and it had healed satisfactorily. A youth of 17 was also shown who had sustained a grossly displaced fracture of the upper end of the tibia, with damage to the popliteal artery. The artery had been explored, the damaged part resected, and an end-to-end anastomosis performed 14 hours after the injury. Full restoration of the circulation had been achieved and there was no definite ischaemic abnormality in the leg.

Mr. R. H. C. ROBINS presented four cases of paralytic scoliosis. He discussed the problems of treatment, particularly those arising in connexion with spinal fusion. Mr. CAPENER presented three cases of the antero-lateral approach to the spine in tuberculosis and for biopsy of the vertebral bodies. Cases were also shown by other members of the hospital staff. All were of considerable interest, not only to orthopaedic surgeons but also to general practitioners. They gave rise to friendly, lively, and informal discussion.

After lunch members toured the hospital and saw an exhibition. This included a demonstration of the transition from an apparently innocent lesion of bone to one which had malignant potentialities, and reviews of 81 slipped upper femoral epiphyses, 76 cases of cervical-spine fracture dislocations, and 30 paralytic dislocations of the hip. Also shown were some unusual carpal injuries, fatigue fractures of the femoral neck, cases of hand injuries, and of osteitis fibrosa cystica.

After the meeting members were very kindly entertained by the president and Mrs. Capener at a garden party in the beautiful grounds of their home at Haldon Grange (for a notice of this see *Supplement*, July 2, p. 24).

SECTION OF ANAESTHETICS

Thursday, June 23

Obstetric Analgesia

With the president of the Section, Dr. W. ALEXANDER LOW (London), in the chair, the meeting opened with a symposium on obstetric analgesia.

Pudendal Block

Dr. E. H. SEWARD (High Wycombe) discussed the use of pudendal block. He said that it was a suitable form of regional analgesia for the great majority of vaginal obstetric procedures. It might be considered desirable whenever one wished to avoid the dangers of general anaesthesia. The technique was easily mastered and was suitable for domiciliary and institutional use where facilities were limited. It might be carried out as a nerve block in the vicinity of the ischial spine, or by a more widespread infiltration covering the relevant nerves as they travelled across the pelvic floor. Dr. Seward recommended the technique of injection per vaginam with a finger guarding the needle throughout the greater part of its length. Although the method was safe and simple to perform, the main dangers were those of breaking the needle and of inadvertent intravascular injection. 1% lignocaine hydrochloride would produce analgesia within three minutes and this should last for one hour. The addition of adrenaline 1 in 200,000 was advised, but hyaluronidase had not been found useful.

He concluded that pudendal analgesia should be used more often, and this might be encouraged if the practitioner performing a pudendal block and the operative delivery was entitled to a fee for the block instead of being recompensed only for the materials used.

Inhalation Analgesia

Dr. R. BRYCE-SMITH (Oxford) discussed the use of inhalation analgesia. He suggested that inhalation analgesia by itself was rarely sufficient, and must be combined with the use of a continuously acting drug such as pethidine, which raised the pain threshold. Such a technique could be effective if scrupulous attention was paid to detail, and if both the mother and attendant appreciated the meaning and use of general analgesia. The stages of labour were accompanied by different patterns of uterine contraction, and consequently pain. These must be recognized so that inhalation might be started a sufficient time before pain was felt. Careful assessment of the course of labour also allowed the maximum period of freedom from pain by the use of long-acting drugs before inhalation became necessary.

Nitrous-oxide–air machines often fell short of individual requirements, and delivered an anoxic mixture which precluded their use in foetal distress and in some cases of maternal disease. Alternatively, 0.5% trichlorethylene in air from an approved inhaler would prove efficient for up to 5–6 hours, Thereafter, further inhalation on top of the accumulated trichlorethylene could cause anaesthesia rather than analgesia. In hospital practice 75% nitrous oxide and 25% oxygen could be used under medical supervision, and the degree of pain relief was comparable to that of 0.5% trichlorethylene, and superior to that of 50% nitrous oxide in air.

Dr. Bryce-Smith felt that many of the failures of analgesia were due to ignorance and lack of interest in an aspect of labour which should be as important as the delivery itself. Thus success or failure largely depended on the attendant rather than the technique. This applied not only to a knowledge of the method, but to the application of understanding, encouragement, and humane nursing of the patient.

Caudal Analgesia

Dr. A. H. GALLEY (London) spoke on caudal analgesia in obstetrics and recalled the fact that the technique had been used for every obstetric procedure in which relaxation of the uterus was not required. Nearly twenty years ago Hingson and Edwards introduced this technique in the U.S.A. for the complete relief of pain during childbirth. Soon afterwards Galley and Peel introduced the method into the United Kingdom. Dr. Galley listed the indications and contraindications, and described the methods used, but complained that the technique still suffered from the fact that there were no positive signs that the needle was safely placed in the caudal canal. Three negative tests were therefore of the utmost importance: the withdrawal test to ascertain that the tip of the needle had not pierced the terminal dura; the air test to ensure that the needle had not slipped dorsal to the sacrum; and the use of the test dose, which made it almost impossible to induce mass spinal analgesia by mistake. Both needles and plastic catheters had been known to fracture while in the caudal canal.

Dr. Galley had made inquiries from 124 anaesthetists and found that only 17% were regular users of the technique. The reasons for this lack of popularity were that the induction and supervision took up too much of the anaesthetist's time, particularly during its use as an analgesic during childbirth. Moreover, alternative techniques had improved during the past decade and were also safer than heretofore for both mother and child. The speaker admitted that his personal reasons for not using the technique more often were that it was too time-consuming and that it immobilized one of an anaesthetic team for anything up to 12 hours. It had also become the practice in King's College Hospital to reserve the technique for cases of cardiac or respiratory insufficiency which necessitated the minimum of strain on the mother during labour.

Drug Effects

Dr. C. A. FOSTER (London) spoke on the effects and dangers of drugs used for obstetric analgesia. He said that the ideal drug should give complete freedom from pain, mental relaxation, allow a normal spontaneous delivery, and be without toxic effect on mother or foetus. Morphine was considered of use only as a yardstick for other drugs. Although pethidine was similar to morphine, it was a much weaker drug, and when combined with an antagonist had proved a valuable agent. Dr. Foster admitted that little scientific knowledge of the ataractic drugs existed. Chlorpromazine by itself was unpredictable and might cause hypotension, depression, and full memory of pain. However, mixed with other drugs, many of its more valuable effects were seen. The speaker concluded by suggesting that the ideal has not yet been attained, but the most promising combination of drugs appeared to be pethidine and promethazine and scopolamine, with or without an antidote to the respiratory depression produced by pethidine for the first stage, supplemented by nitrous-oxide–oxygen for the end of the second stage.

The discussion at this symposium was opened by Dr. P. J. HORSEY (Southampton), who suggested that all anaesthetists should learn the technique of pudendal block and teach general practitioners. Although the block was more commonly performed by obstetricians, there was a place for an anaesthetist in every labour ward to supervise whatever form of analgesia was used. Dr. FLOOD (London), Dr. J. G. BOURNE (London), Dr. H. C. HILL (Torquay), Dr. G. M. R. HOLLIDAY (Plymouth), Dr. W. N. ROLLASON (Aberdeen), and Dr. FRANKIS T. EVANS (London) also took part, and the original speakers replied to questions.

Anaesthesia in the Aged

With a vice-president, Dr. FRANKIS T. EVANS (London), in the chair, Dr. B. R. J. SIMPSON (Oxford) presented a paper on the effects of anaesthesia in the aged. He described a survey which was undertaken to establish the size of the problem of mental and personality deterioration resulting from anaesthesia and elective surgery in old people. During 1959, 741 patients aged 65 or over were admitted to hospital for elective surgery and were interviewed in their homes before and after operation. In addition, psychometric analysis was performed on 239 of these by an experienced

geriatric psychometrist (Dr. Moyra Williams). The information was classified by a scoring check sheet which measured the functions of self-help, physical activity, mental activity, memory, personality, and emotional state in five grades. These ranged from full and unaltered function in grade 1 to vegetative existence in grade 5. Improvement or deterioration after operation was recorded if a change of function occurred sufficient to move a patient up or down one or more grades in any of the function groups.

General anaesthesia was given to 484 patients and local analgesia to 139; 58 were subjected to neither anaesthesia nor surgery. Sixty patients died and were excluded from the analysis. Thirty per cent. were better after operation and 8.5% worse. No gross dementias occurred. The patients who were made worse post-operatively fell into two main groups: (*a*) those with deterioration as a result of progression of symptoms from the condition for which surgery was undertaken (50 patients, of whom 38 received general analgesia and 12 received local analgesia); and (*b*) those showing deterioration owing to inevitable progression of disease processes unconnected with the condition for which surgery was undertaken (35 patients, of whom 20 received general anaesthesia and 15 local analgesia). One patient suffered as the result of inadequate post-operative care, but no satisfactory explanation could be found for the deterioration shown in three others, only one of whom had received a general anaesthetic. It was concluded that these patients who became worse could not be regarded as a lesser degree of the organic process responsible for "gross dementia syndrome."

Dr. Simpson described the statistical analysis allowing 40 variables for each patient and found these results reached two main conclusions: (1) Anaesthetics had no effect whatsoever on mental state. (2) Patients who had operations which relieved symptoms improved in respect of their adequacy in their daily lives.

Dr. J. G. BOURNE (London), Dr. A. H. GALLEY (London), and Dr. W. N. ROLLASON (Aberdeen) took part in the discussion which followed.

Intractable Pain

Dr. R. P. W. SHACKLETON (Southampton), a vice-president, then took the chair, and Dr. P. R. GAVIN (Taunton) presented a paper on the alleviation of intractable pain. He said that in recent years there had been a reawakening to the need for a new approach to intractable pain. This might have come about partly from the increased longevity of the human race in highly civilized societies and partly from the increasing facilities for treating the conditions to which the aged were especially prone. The use of analgesic drugs had long been, and no doubt would continue to be, in the forefront of pain therapy. Many specific analgesics, some comparatively long-acting, were replacing our old ally morphine and its derivatives. Almost without hypnotic action, these potent drugs could control severe pain without affecting the mental processes, thus allowing a normal daily life. Amongst these, oxycodone pectinate and dextromoramide were particularly worthy of consideration.

Pain arising from new growths or other abnormal conditions could be isolated from the appreciation centres by blocking afferent pathways. Surgically, this could be achieved in ascending order of refinement by section of peripheral nerves, posterior rhizotomy, or cordotomy. However, many patients were unsuitable for neurosurgery and some less disturbing alternatives must be sought. Intrathecal injections of alcohol had been used occasionally since 1931. They were intended to damage the posterior roots which affected pain, but spared the more resistant motor fibres. More recently phenol in heavy solvents had shown great promise in both selectivity and control, particularly in the treatment of intractable pain of malignancy and of painful spasm or spasticity occurring in neurological diseases. The possibilities of this approach deserved to be more widely known.

Dr. Gavin said that the development of clinics specifically for the treatment of intractable pain was a comparatively new, but nevertheless promising, step towards the control of man's oldest affliction. The study of this condition soon revealed that when a severe chronic pain was relieved life was almost certainly prolonged, and this should be the foremost aim of progressive medicine.

The discussion was opened by Dr. R. P. W. SHACKLETON, and Dr. W. P. GRIFFIN (London), Dr. A. H. GALLEY (London), and Dr. B. R. J. SIMPSON (Oxford) took part.

SECTION OF DERMATOLOGY

Thursday, June 23

Latest News on Skin Diseases

With the president of the Section, Dr. G. B. MITCHELL-HEGGS (London), in the chair, Dr. A. J. ROOK (Cambridge) opened the symposium on "The Latest News from Town and Country on Skin Diseases" with an account of dermatoses due to plants. There were three varieties of plant dermatitis. First, primary irritant dermatitis when the plant exerted a directly injurious action on the skin, stings by the stinging hairs of the nettle offering an obvious example; secondly, and the most common, an allergic sensitization; and, thirdly, a light sensitization dermatitis. The hazards from plants were changing. Many more people were keeping indoor plants and small greenhouses were much more common. New varieties of plants were being introduced. The nature of the antigenic substances in plants causing allergic sensitization was complex. Most belonged to the terpenes and glucosides, but their individual biochemical identification was difficult owing to their complexity, but was being proceeded with. They were usually secondary products and did not enter the metabolism of the plant. The pattern of the dermatitis depended upon the potency of the antigen, the quantity contained, and its site in the plant. Plants causing dermatitis classified botanically were restricted to relatively few families. The clinical picture was not specific and many patterns were seen. Diagnosis depended on clinical history, the identification of the plant, and the confirmatory positive patch-test (here caution to avoid primary contact must be exercised). Treatment included avoidance of the particular single plant which was usually alone responsible. Desensitization was not practical. Phytophoto-dermatitis manifested itself as bullae, often striate or irregularly linear in shape, on areas of contact between leaves or stem and the skin 12–24 hours later and following exposure to the sun. The bullae soon healed, but there was residual pigmentation. These cases often aroused alarm and had even been attributed to exposure to mustard gas.

Dr. H. R. VICKERS (Oxford) gave an account of cutaneous infections acquired from animals. The virus diseases included cowpox, milker's nodes, and orf. Cattle infected with cowpox had warty nodules on their teats; in man the lesions usually occurred on the hands. The primary lesion was a vesicle with at first clear but later turbid fluid, which rapidly became umbilicated. After 10 to 14 days the area became scabbed. The lesions of milker's nodes occurred in man as well-defined pea-sized, reddish-blue, firm, and slightly tender nodules which lasted 6–9 weeks. Orf, derived particularly from sheep and goats, in man formed papules which became umbilicated; the course was several weeks. Foot-and-mouth disease was rarely seen in man. Lesions occurred in the buccal cavity, and sometimes a picture resembling a severe erythema multiforme might be produced. Cat-scratch disease was probably commoner than was recognized. An indurated nodule persisted for several weeks at the site of a cat scratch. This was accompanied by marked regional adenitis and constitutional disturbance. Anthrax and erysipeloid were bacterial infections. Erysipeloid usually attacked the hands and was characterized by a well-defined, raised erythematous area. The fungi derived from animals infecting man were *Microsporum canis* and *Trichophyton discoides* and *mentagrophytes*. Amongst arthropods, mites causing scabies were the most important. Mr. J. A. DALL (Torquay) described the cutaneous infections in animals

communicable to man, and illustrated his account with excellent colour photographs. In addition to the diseases mentioned by Dr. Vickers he thought that tuberculosis of cats might be a hazard.

Griseofulvin

Dr. D. I. WILLIAMS (London) gave an assessment of the value of griseofulvin in the treatment of ringworm now that more than one year's experience and many publications on its use were available. First and foremost, all forms of scalp ringworm responded well, including favus, and *x*-ray epilation was no longer required. A dose of 1 g. a day for four to five weeks was required for most cases. In other forms of ringworm, local treatment alone might be successful, but in resistant *Trichophyton rubrum* infections involving glabrous skin and nails griseofulvin was now the treatment of choice, though cure was still difficult to achieve. Toxicity from griseofulvin had not been encountered.

Dr. MITCHELL-HEGGS emphasized that griseofulvin should probably not be used until microscopical and preferably cultural identification of the fungus had been done. Dr. WILLIAMS felt that the disability produced by ringworm of the nails justified long courses of griseofulvin. Dr. VICKERS told of one patient who developed a syndrome of a collagenous type of illness after griseofulvin, but one could not be sure it was caused by the drug.

Allergic Granulomata

Dr. I. B. SNEDDON (Sheffield) discussed allergic granulomata of the skin. These granulomata showed a distinctive pattern of histiocytes (called epithelioid cells in error because they resembled epidermal cells). The histiocytes might fuse to form giant cells which, in the characteristic foreign-body reaction, had nuclei disseminated through the cytoplasm, but often there were Langhans giant cells with nuclei round the periphery. He had been able to induce a granuloma with a sarcoidal-like reaction by patch-testing a patient, suffering from berylliosis, with a solution of beryllium, thus proving the allergic nature of the disease. Likewise, the cutaneous papules that occurred in the axillae of patients after using deodorant sticks containing zirconium had been shown to be the result of allergy to zirconium. Sarcoidosis, however, had not been experimentally produced by any allergen. Reactions following exposure to silica, after a varying latent period, were probably the result of an alteration in colloidal state of the silica and not due to allergy.

Dr. C. D. CALNAN (London) reported three new types of industrial skin hazards. Aluminium was being used instead of copper for electric cables, and special new fluxes, required for jointing the aluminium, were producing contact dermatitis. Rubber-based adhesives, for use with leather as in the shoe and handbag industries, had been improved by formaldehyde resins. The most widely used resin, a paratertiary butylphenol formaldehyde one, was producing an allergic contact dermatitis. New methods for copying and duplicating that had recently been introduced might also cause dermatitis, not only in those operating the copying machines, but also in those who handled the paper and who manufactured the materials used.

SECTION OF GERIATRICS

Friday, June 24

Occasional Papers

Dr. C. T. ANDREWS (Truro), a vice-president of the Section, took the chair for the second session, at which five papers were read.

Bronchitis in the Elderly

Dr. F. J. FLINT (Sheffield) discussed bronchitis in the elderly. The picture was one of excessive mucus secretion and deformity of the bronchioles with obstruction. Bronchial spasm was a factor of little importance in the elderly; bronchial asthma itself was rare. Cor pulmonale was a common sequel in younger people, but a rare one in the elderly. Besides the usual presenting signs there might be mental confusion, stupor, dehydration, uraemia, or bizarre chest pain, but fever was often absent.

It was hard to distinguish cardiac from respiratory dyspnoea. Dr. Flint demonstrated the Wright peak-flow meter, which could help to make the distinction. Expectorants, bronchodilators, and most other commonly advocated measures were ineffective: if oxygen was given it was best used as a 4% mixture in air. The important organisms were the pneumococcus and *H. influenzae*, for which he advocated penicillin, or chloramphenicol in severe cases.

Dr. J. H. SIMPSON (Exeter) wondered if CO_2 narcosis was really so common as supposed. Dr. FLINT, in reply, advised watchfulness in giving oxygen to any drowsy patient, and deprecated sedatives where there was cyanosis.

Diagnosis of Myxoedema

Dr. W. H. LLOYD (Oldham) spoke of the difficulties of diagnosing myxoedema in the elderly, which was a common disease with a rising incidence with age; it was insidious and showed protean manifestations. Periorbital puffiness and "squaring" of the face were helpful signs; so were the voice changes, which he illustrated by tape recordings before and after treatment. The diagnosis could be confirmed by the response to treatment, so serial investigations, especially weight- and voice-recording, and colour photography were required. He used L-thyroxine in treatment: dosage had to be carefully graded, especially in cases with heart failure.

Dr. T. S. WILSON (Redruth) wondered how commonly mental confusion accompanied myxoedema. Replying, Dr. LLOYD suspected that many cases might be found undetected in mental hospitals.

Diabetes in the Elderly

Dr. T. S. WILSON (Camborne) next discussed the treatment of diabetes in the elderly. The peak age of onset was 55–60. Many cases were being overlooked, and, though the disease was usually mild, the complications were as common as in the severer diabetes of younger people. He advised as little change as possible in diet unless obesity was a problem. When insulin was necessary, dosage must be simplified; anyway, the capacity for self-administration fell off with age. In uncomplicated cases oral drugs were ideal. He had found gangrene in 4.5% of 738 cases. Listing the indications for operation, he considered amputation should be through the mid-thigh in most cases.

This point was taken up in the discussion, Dr. ANDREWS, the chairman, holding that most gangrene with diabetes was in reality arteriosclerotic. Dr. LLOYD said he had often, without anaesthetic, amputated through gangrenous tissue close to the line of demarcation with good results.

Chronic Arthritis

Dr. F. M. LUCAS (London) presented a paper on the management of the chronic arthritic case on behalf of Dr. MARJORY WARREN (London), the Section's president. The aim was to provide the patient with all possible means of becoming independent and remaining so. She reviewed the need for special sticks, correct footwear, loose and easily manipulated clothing, and gadgets of all kinds to help in dressing, toilet, and feeding. In particular, chairs must be of correct height and design, and wheelchairs adapted to individual needs.

Dr. A. N. EXTON-SMITH (London) considered there was a special need for chairs adjustable for height.

Cardiac Problems in the Elderly

Dr. JOHN N. AGATE (Ipswich) then spoke of the pitfalls of diagnosis in cardiac states in the elderly. Signs did not always mean just what they meant in younger people. Ischaemic heart disease was common but was seldom associated with pain; cardiac infarction was often "silent,"

presenting instead in a variety of unexpected ways, even as a confusional episode or as a hemiparesis. For this reason routine electrocardiography was valuable. Heart failure was often hard to diagnose, and ankle oedema was especially misleading in the elderly. Nevertheless the prognosis of failure was often good with early and effective treatment, so there was no excuse for therapeutic inactivity because the patient was old.

Finally, Dr. Agate made a plea for the abandonment of the terms "myocardial degeneration" and "senile myocarditis," for these were not entities and their clinical use often caused other remediable conditions to be overlooked.

Dr. ANDREWS agreed that cardiac ischaemia in the elderly was not synonymous with cardiac pain. Dr. FLINT believed that the many patients who died with large hearts which showed no fibrosis, and who had had no clinically demonstrable hypertension, had nevertheless formerly been hypertensive subjects, whose hearts eventually failed to maintain this tension.

CRIME AND SIN

SIR JOHN WOLFENDEN AT WINCHESTER

This year's "Winchester Address" was delivered on June 23 by Sir JOHN WOLFENDEN, Vice-Chancellor of Reading University, to a large audience at Winchester, under the chairmanship of Dr. JOHN HAPPEL. Sir John discussed the approach to its task of the committee that bears his name, under the title "Crime and Sin." The address is sponsored by the Winchester Division of the B.M.A.

After some introductory remarks Sir JOHN WOLFENDEN said that when Sir David Maxwell Fyfe put this obligation upon him the first thing to be done was to arrive at a decision about the constitution and composition of the committee. He thought it ought to be a departmental committee and not a Royal Commission for two reasons. If it were a departmental committee the job would be done more quickly. The second and more valid reason was that evidence submitted to a Royal Commission had to be published, and it seemed to Sir David and to him that they would find out more if there was no obligation to publish the evidence afterwards: a good deal of the evidence would not have been received had publication been a condition.

Wolfenden Committee's Tasks

Having described the composition of his committee, Sir John said he began its work by making two observations: "The first was that it was our business as I understood it to act as an intelligent jury. We are not supposed to be experts; there was no reason to suppose any one of us was particularly informed or experienced in either of the two topics. We were simply an intelligent jury and it was our business to listen to the evidence presented and, on the basis of that evidence, to exercise our own judgment and our own consciences. It was not the least use our looking over our shoulders all the time about what anybody might say, what the press might say, what the public might say, about whatever it might be we eventually recommended." The second observation was that he hoped they would produce a document which, though nominally an official report to two Secretaries of State, would nevertheless be something which any intelligent interested person would be able to read.

Their problems were complicated by the fact that they were dealing not only with the Home Secretary but also the Secretary of State for Scotland. The presence of Scotland added enormously to the complications; not only because of reasons of Scottish nationalism, but also because in this particular matter the law of Scotland differed in important aspects from the law in England. "All the time we had to have in mind that whenever we arrived at some conclusion we suddenly had to stop and take a breath and say, 'How does this work with Scotland?'; and then either put a note in saying, 'See para. 99' or, 'The situation in Scotland is quite different'; or else, in the last resort, put in a note stating, 'This applies, *mutatis mutandis*, to Scotland.'"

Sir John continued by saying that he would take one or two major principles out of what they had tried to do. But it was important to remember what their terms of reference were, and especially what they were not. They were told to investigate and to make recommendations about the law and practice relating to offences arising in connexion with prostitution and homosexual offences as well. They were concerned with the law and practice in relation to these two subjects, and were not there to write a book of the twentieth century about prostitution as a social evil or sociological phenomenon. They were not concerned with prostitution, as such, but with offences against the criminal law arising out of prostitution. They were not there to write a book of the twentieth century and its homosexuality; they were not concerned with homosexuality as such; this was sometimes forgotten in the criticism made about the committee and the comments made on the report.

Homosexual Behaviour

Homosexuality was the condition in which a man or a woman behaved homosexually. It occurred perhaps most often as a result of the state or condition of homosexuality. Homosexual behaviour was not necessarily confined to men or women who were homosexual. One thing he had learnt was that it was a great mistake to think that the human race could be divided into two clear categories: on the left those who were homosexual, and on the right those who were heterosexual. There was an almost infinite gradation along the line towards something approaching 100% heterosexual and something approaching 100% homosexual. "Our concern was primarily with homosexual offences."

Thirdly, Sir John said, they were not there to write a book on moral theology. It could be said it was not to be their business to consider the moral ethical judgment that anybody might care to make about prostitution and offences connected with it or homosexual offences. They were there to talk about the law and practice.

What is Crime?

After discussion with Lord Goddard and other distinguished High Court Judges, he had found the legal attitude on crime was somewhat as follows. There was no form of behaviour in this universe which was *per se* and of its own nature criminal. A form of behaviour was criminal when the competent legislative authority had said about it, "If you do that we shall punish you." That was what constituted crime, and whether the competent authority was Parliament or a headmaster of a school or the chairman of a distinguished professional body, provided it was a competent legislative authority, if that person or body said, "If you do that we shall punish you, and these are sanctions

and this is the authority we have over you "—from then on, it was crime.

"Well, that to me ought not to have been anything very startling. But I am afraid it was. Because I had not taken in the lesson I ought to have learnt as a headmaster. . . . I cherished a sort of idea—and I think a lot of people do if they have been put in authority over a lot of other people—that, if only one could get it right, one could so legislate that one's own moral pattern of the good life was almost inevitably led and followed by those who obeyed the rules one made.

"Now I ought to have learnt about this—and I had not. I ought to have learnt from one very nasty small boy. One day the very nasty small boy was brought into my study by an infuriated form master, metaphorically by the ear—all the boy had done had been the ordinary thing—copy answers of Latin grammar off the boy next to him or something in the normal way. It was quite obvious, there was no doubt about it, and he was obviously 'for it.' Obviously he was going to get it, but before he got it I had to go through the motions of asking if there was anything he wanted to say.

"He said, 'Yes'—I said he was a very nasty small boy. He said, 'Sir, there is no school rule against it.'"

Unless you legislated about every possible thing there was to legislate about, Sir John continued, there was always the nasty small boy's evidence. And, alternatively, if you did legislate about every single thing there was to legislate about, what you would in fact do was destroy personal responsibility. No form of behaviour in this universe was of itself criminal. It was only criminal when you made it so.

Where did they get? They were plainly in a society which had rules—whether a State or a school—a certain number of forms of behaviour which had been explicitly made criminal. You could narrate them, because they were set down in rules and statutes and regulations.

Overlap with Sin

The word sin plainly implied certain theological and religious convictions, and for those who held those convictions the word sin had meaning. But, of course, it had to be recognized that to a very large proportion of our fellow countrymen these religious and theological presuppositions were not acceptable, and so the word sin to them meant little or nothing. But if the word sin was a bit too stark, quite a lot of our fellow countrymen and women would agree to the use of some adjectives of criminality. On whatever basis their views were founded, whether humanistic, evolutionary, hedonistic, altruistic, or economic, or just fashion—some basis somewhere—a great many people were prepared to use the words "right" and "wrong," without the implication of sin, but just ethical words. People were prepared to say certain classes of behaviour were "not right." Whether you called it "sin" or called it "wrong" or "not right."

"Do you see my problem? Do you see why I asked Lord Goddard what sort of actions ought to be crimes? How many of those classes of behaviour which quite a lot of people, the majority of people, would regard as falling in the moral or ethical sphere of adjectives, ought to be included in the criminal law so that they become crimes? That is what I was really trying to do."

Distinction had to be made between crime and sin. There were actions which properly had attached to them adjectives of morality, and there were actions which had properly attached to them adjectives of criminality. "How many of these ought to be made those?"

There was a middle line of actions recognized by most people as being wrong, and those same actions had also by legislative authority been made into crimes. To that extent they overlapped. Obvious things like killing and stealing, and those things which were recognized as being wrong from a moral point of view, were also criminal. And there was a very large overlap there. But there was by no means complete identity. The overlap was nothing like complete. On the one side there were a certain number of actions which the legislature had said were crimes, and about which he, at any rate, did not feel any very full or deep moral guilt.

Riding a bicycle at night without a red rear-reflector obviously was a very inconsiderate thing to do, and it was antisocial and could have very serious consequences. But did they really regard it as very shameful morally? It was, of course, an offence against the law. There were all sorts of things like that which it was a good thing to discourage, but which he, at any rate, felt no very severe guilt about. On the other hand—and this was where the shoe began to pinch—there were quite a lot of ways of behaviour, which at any rate a large number of people would regard as morally reprehensible, which were not, in the present law of this country, crimes.

Sexual Morality and Crime

In the particular field of sexual morality, this was rather a curious inconsistency. There were, Sir John supposed, four standard forms of extramarital sexual behaviour—fornication, adultery, homosexual behaviour between men, and homosexual behaviour between women. He thought most people would feel these four ways of behaviour were all in greater or less degree morally reprehensible. Of these four ways of behaviour one—and only one—was a crime. The other three were not. You could not send anyone to prison for fornication, or adultery, or homosexual behaviour between women. But you could for homosexual behaviour between men. Why? What sorts of action ought to be crimes? On what grounds were three of these forms of behaviour not recognized by the legislator as crimes, while one was? On what grounds?

It depended on the grounds upon which they thought the law ought to support, buttress, fortify the moral view. And that depended in turn on how far they thought that moral adjectives applied to this form of behaviour or the other, and on what grounds. He would be prepared—on the grounds of human living together and human happiness and human unhappiness, which in practice the large majority of people took as their basis of approval or disapproval of ordinary human behaviour—on that sort of basis, he was prepared to say that adultery and its consequences produced far more human unhappiness than homosexual behaviour between men, adults, in private, ever could produce.

Sir John said he did not know why there was this particular legislation about this particular form of extramarital sexual life. He was not clear what it was the legislator had tried to do when he was legislating about behaviour in that sort of field.

The Public Good

It was difficult to say what anybody meant by moral responsibility, or by personal responsibility of any kind. Short of that, the legislator was concerned about what could properly be called the public good.

There were all kinds of different moral standards prevalent in different parts of the world. In this country there had been different moral standards down the centuries. "Which ones are you going to try to make the law identical with? And if you get to the point at which it is supposed the moral adjectives and criminal adjectives mean the same thing, and it is supposed that morality and its adjectives and criminality and its adjectives are really synonymous (and some people think that), if you really believe that—then we are in the most frightful difficulty in making morality mean anything at all.

"I don't mind when I cross a frontier from one country to another, moving from one set of laws to another, and I try to obey the new ones. But if it is seriously maintained that the laws of the country represent and are identical with the morality of the country, then, bless my soul, I should find it hard to change my way of morality when I cross a national frontier.

"I must be dogmatic for the sake of brevity. I find it hard to accept the view that legislation about these moral adjectives does anything but destroy the moral adjectives themselves. Back to the nasty small boy again. If there had been legislation about everything, if there had been a whole string of rules, if a nasty small boy cannot err, what exactly is he doing? Is he, in fact, ever behaving morally at all?

"When you drive a motor car through a restricted area at 29 m.p.h., why do you drive at 29 m.p.h.? Do you because you

believe it would be morally wrong to drive at 31 m.p.h. ? And, if so, who made it morally wrong to drive a motor car at 31 m.p.h. in one place and not in another ? Do you do it because you believe it morally wrong or because you believe if you drive at 31 m.p.h. and get caught you will be for it ?

"If by any chance it is the latter, then I suggest your reasons for driving at 29 m.p.h. are not moral reasons, they are simply prudential.

"If you tell me then that it is a moral duty to obey the law then I have only two replies. It is a moral duty to obey which law ? The law in operation to-day or in operation 50 years ago ? Or the law which is going to be in operation 50 years hence ?

"My second answer. While you tell me it is a moral duty to obey the law, what do you do about bad laws ? On the first of these two reasons we have to be careful because, in the sphere we are talking about, there is an apposite example."

Homosexual behaviour between adult consenting male persons in private, with the exception of one form of this behaviour which had been an offence against Canon law, was an offence against criminal law—ever since homosexuality between consenting males in private became an offence in this country about 70 years ago. It was not the case that this sort of behaviour had been against the law for the centuries. It became an offence, in private, 70 years ago. Was it therefore permissible morally to do this sort of thing up to 1879, and did it then become impermissible morally from 1880 onwards ? Could you have retrospective immorality ?

Personal Responsibility

To try to equate completely the moral sphere of judgment with the criminal and legal sphere was involved. In practice and in actual life should the legislature try to protect, buttress, fortify a general sort of vague broad national conscience ? There was one important element in the public good that they overlooked at their peril, that it was an essential element in the public good that there should be private personal responsibility. "If you legislate only quantitatively a man's private personal responsibility which you bring within the realm of the criminal law, to that precise extent quantitatively you decrease the area of his personal responsibility."

Sir John's own view was that over the last 30 or 40 years there had been quite enough diminution of personal responsibility in this country, and so far from encouraging this we should be trying to stop it. The more you legislated the more you impaired personal responsibility. He had been brought up, and so had all of them, in what he still thought of as the good old-fashioned tradition of English political theory—that you legislate as little as you dare. You had to legislate of course to stop people killing each other, you had to legislate to stop people stealing other people's possessions. But at your peril did you legislate more than you must. The more you legislated, *pro tanto* you diminished the area of personal responsibility. That really was putting back the problem on to the legislator. But that was where it belonged. It was the legislator who made things to be crimes.

Sir John said he had gone to a school where he came across two whole pages of records of names of boys who had been expelled for ever from the school—because they had been caught smoking in the school train. Smoking in school was a good example of man-made crime. By the time he stopped being a legislator in a public school, he had learnt the lesson of the nasty small boy, that school rules should be (*a*) as few as possible, (*b*) those that were should be enforceable, and (*c*) that, school rules being enforceable, however few they were should be enforced. Because, as they all knew, it was the certainty of apprehension rather than the weight of the penalty which deterred. That was the right attitude, nationally, about legislation.

Clear Thinking

A clergyman had told him that this was all logic-chopping and sophistry. The clergyman had said the answer was perfectly plain: the root of all morality and the root of all law was to be found in the Ten Commandments. But if you looked at the Ten Commandments dispassionately, how many were embodied in the law of this country ? Either three and a half or four and a half according to how you defined "to bear false witness." It was simply not the case that there was identity between the adjectives of morality and adjectives of criminality.

It was desirable to be clear about this definition. A very distinguished cleric was talking about it. He was by way of agreeing with part of the report on homosexuality, but strongly disagreeing about part of the findings arising from prostitution on the ground that, as he said, they were blaming it all on the woman. Was not the customer of the prostitute just as guilty as the prostitute ? How could they, said he, reconcile themselves to this double standard of morality ? Of course the man was just as guilty as the prostitute of the sin of fornication. But he was not as guilty as the prostitute of the offence against public order and decency. That was a criminal offence.

There was a terrible ambiguity about guilt. Was one guilty of a moral or criminal offence ? In view of the respective guilt of these two people, it was important to recognize the distinction between the two offences. How far was it right, how far was it desirable, how far was it damaging to public good to bring them together again so that they overlapped, and how far ought they to overlap ? They were not concerned with moral theology.. They were concerned with talking about the law and about crime.

ECLAMPSIA AND PRE-ECLAMPSIA

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY

[FROM SPECIAL CORRESPONDENTS]

The International Society of Geographical Pathology held its seventh international conference from June 28 to 30 at the Royal College of Surgeons, Lincoln's Inn Fields, under the chairmanship of Professor J. H. DIBLE. On the first two days the conference discussed eclampsia and pre-eclampsia, and on the last day there were contributions on other topics (not reported here).

Geographical Incidence of Eclampsia

The first session comprised reviews of eclampsia and pre-eclampsia from each of the participating countries. Dr. T. F. CORKILL (New Zealand), speaking for both his own country and Australia, said that in the period 1928 to 1958 there had been a marked fall in the incidence of eclampsia, from 3.2 to 0.8 per 1,000 deliveries. Further indications of a decrease in severity were that most convulsions were now occurring in the second stage of labour, and that the total death rate from toxaemia had fallen tenfold over this period. These advances could be attributed to better recognition and better social services rather than to any advance in therapy. Similar findings were reported by Dr. L. RAURAMO from Finland, where the incidence in the years 1927 to 1958 had fallen from 4 to 1.5 per 1,000 deliveries. Professor P. JAKOBSSON (Iceland), emphasizing the difficulties in making comparisons, said that few mothers in his country came to hospital before the 20th week and so the toxaemia rate was very high (7.2%).

Professor A. BRZEZINSKI (Israel) compared the incidence of toxaemia in four areas—Beersheba in the Negev desert, Jerusalem in the Judean hills, Tel-Aviv on the coast, and Affulah in the north: 96% of all births in Israel took place in hospitals, he said. The total rate for toxaemia in the whole country was 1.4%, but the highest incidence was in the north (2.7%) and the lowest in the south; with Jerusalem and Tel-Aviv in between. Analysing the data by race, the highest incidence was in women of Israeli stock, then in those of American–European descent, and the lowest in Afro-Asians (excluding Iraqis). This difference was present in all

four areas, but part of the difference in the four areas could be explained by the preponderance of Afro-Asian Jews in the south of the country. Coronary artery disease was also less common in these communities than in others. There was some seasonal trend in the incidence of toxaemia in all four centres; the highest incidence was in the first three months of the year. Professor F. TAKAKI (Japan) showed that in Japan the picture to be seen was different from in the Western countries. Over the past few years there had been a gradual increase in the incidence of eclampsia rather than a fall. Evaluation of data in Japan was, however, difficult, as most deliveries occurred at home. Dr. J. L. MASTBOOM reported a fall in the Netherlands in the incidence of both eclampsia and the maternal mortality due to it. In the period 1920–40 the mortality had shown little change (40 per 100,000 live births), but since 1940 there had been a steep fall (to 10 per 100,000 live births).

Eclampsia in the Negro

Dr. J. B. LAWSON (Nigeria) said that in his country eclampsia was still a minor problem, and accounted for less than 10% of all maternal and perinatal deaths. The average blood-pressure of African women before the 20th week of pregnancy was 105/65, and therefore for them a rise of 30 mm. Hg systolic and/or 15 mm. Hg diastolic was a better indication of pre-eclampsia than an arbitrary level of 140/90. No correlation with season or weather was found, but this was complicated by migration of the population at risk. In certain tribes, where fattening of brides had once been practised, eclampsia had been common, but since the discontinuation of that practice it was now rare. Professor CORALIE RENDLE-SHORT said the incidence of eclampsia and pre-eclampsia was also low in Uganda. In her experience, the onset was much more rapid in Africans than Europeans. Dr. B. V. GAVALLÉR stated that the incidence in Venezuela was 1.8 per 1,000. There was a much lower incidence in private than public patients. In Jamaica Dr. H. G. DIXON had found an incidence of eclampsia of 3 per 1,000, and of pre-eclampsia 6.6 per 1,000. It was similar in both booked and unbooked patients. The highest incidence occurred in September and April, but no definite correlation with weather was found. Perinatal mortality was highest in multiparous mothers. Dr. T. P. MAGEE had studied the incidence of the disease during 1956–8 in the East Indian and Negro communities of Port of Spain, Trinidad. The former, who still kept to their traditional way of life, had an incidence of pre-eclampsia of 27 per 1,000, compared to that of the Negroes of 6 per 1,000, who were adopting European customs. More than one-third of all deliveries were domiciliary and attended by untrained personnel; the perinatal death rate was high, one-third of it being due to eclampsia and pre-eclampsia. Despite this difference in the development of eclampsia in these two races, the incidence of hypertensive disease was almost equal.

Dr. I. MACGILLIVRAY (Aberdeen) showed that the incidence of pre-eclampsia was greatly affected by the different criteria adopted by the various centres. It also appeared from the data collected during this study that the average blood-pressure in pregnant women was lowest at all ages in London, and highest in Northern Ireland and Eire, with Scotland and the rest of England in between. The incidence of proteinuria showed a similar trend. Only when the blood-pressure was greater than 135 mm. Hg was proteinuria common.

Aetiological Factors

The afternoon session was devoted to more general reviews. Professor C. B. F. DAAMEN (Netherlands) stated that the frequence of eclampsia was less in the nineteenth century (1.6 to 1.8 per 1,000) than in 1938 (2 to 3.5 per 1,000). In the first world war there was evidence of a decrease during the war in Germany and Denmark, with a sharp rise after the end. This could have been due to a fall in number of primiparae or to food shortages. This fall was even more marked in Amsterdam in 1944–5, when there was severe nutritional deficiency, with a rise after this. He also pointed out that maternal mortality due to eclampsia had fallen to very low levels in 1957, compared with 1939, except in Japan. He thought that foetal loss was an expression of the severity of the toxaemia.

Dr. R. DOLL (London) gave a general epidemiological account of the results of the survey. In ten countries which reported on more than 1,000 deliveries during the year, the incidence of eclampsia ranged from 0.5 (Switzerland) to 4.1 (Italy) per 1,000 deliveries. The incidence in the United Kingdom was 1.2, and, apart from the two extremes quoted, all figures for incidence were very close, the Belgian Congo and Uganda being similar to European experience. The incidence in "booked" cases was also very comparable (Austria 0.6, United Kingdom 0.5, Australia and New Zealand 1.4). In primigravidae the incidence was 1.5 per 1,000 in the United Kingdom and 3.9 per 1,000 in Australia (being similar for those of Anglo-Saxon and of Italian and Greek origin, despite the difference in dietary habits). The standardized incidence of pre-eclampsia was almost twice as high among primigravidae (11.7) as among multigravidae (5.8–6.9), with no change in incidence with increasing numbers of pregnancies after the first. In order to define pre-eclampsia, data from primigravidae aged less than 30 years and booked before the end of the 20th week were examined. There was a marked correlation between the proportion of women with a high average initial systolic pressure and a maximal pressure of 145 mm. Hg in late pregnancy. This correlation was not so marked with diastolic blood-pressure. In each case Ireland had the highest proportion with high pressures, and Nigeria and Japan the lowest. But in both the latter countries the initial pressure was also much lower in each age group. Comparison of the average changes in pressure recorded in the different countries showed that the response of the cardiovascular system to pregnancy varied from country to country, the extent being unrelated to the initial level and having no obvious relation to diet. The most important factors determining the proportion of women in whom the maximal diastolic rose above 95 mm. Hg were those which determined changes in diastolic pressure in pregnancy, whereas the proportion who developed a systolic pressure greater than 145 mm. Hg depended on factors determining the initial levels of pressure.

Clinical Features

Professor J. C. MCCLURE BROWNE (London) dealt with the clinical aspects of 7,344 primigravidae seen in this country. There had been three maternal deaths, and 11 patients with eclamptic convulsions but no deaths. The mean blood-pressure of these women before the 20th week was 124/73 (upper range of two standard deviations = 148/90) in those aged 15–29, and 127/77 (154/90) in those aged 30–34 years. The mid-pregnancy fall in blood-pressure was not seen. There was evidence that a higher initial level predisposed to a rise only in those over 30. If the systolic pressure was greater than 140 mm. Hg the perinatal mortality rose and the incidence of abruptio placentae fell; for diastolic pressures of over 85 mm. Hg, the incidence of both these conditions rose. Proteinuria was commoner in those under 20 (4%) than in those over 30 (2.98%). Proteinuria affected perinatal mortality: when absent the mortality was 2.4%, when present it was 8.5%. The presence of proteinuria had a greater effect on perinatal mortality in those aged over 20 and for those women with blood-pressures greater than 130/80. The overall perinatal mortality was 2.58%; maternal age itself had little effect, but in those over 30 with a diastolic pressure greater than 90 mm. Hg the perinatal mortality was 12.4%. No clear definition of pre-eclampsia was derived from this survey, but any pregnant woman whose blood-pressure rose above the average (not only the upper limit) should be regarded with suspicion.

Fibrinoid Vascular Lesions

On the second day the morbid anatomy and clinical pathology of eclampsia were discussed. The morning

proceedings were opened by Dr. A. D. T. GOVAN (Glasgow) with a paper on the pathogenesis of eclamptic lesions. His study covered a series of 116 fatal cases drawn from all parts of the world. Before proceeding to the particular lesions he drew attention to the high incidence—25%—of unsuspected pyelonephritis in all age-groups and parities, and the increasing incidence of chronic vascular disease in patients over 30, indicating a need for careful selection of material for study. Of all cases 45% had died of some haemorrhagic catastrophe, cardio-respiratory failure occurred in another 40%, and the remainder died of coincidental disease. A careful study of the cases of cardio-respiratory failure revealed vascular lesions of a nature similar to those found in the first group, thus indicating that in all cases there was a common type of vascular reaction which in its milder degrees took the form of fibrinous vasculosis (see Lendrum*). The lesions were found in liver, brain, and kidney. He suggested that the glomerular lesion with its protein periodic-acid-Schiff-positive deposits was probably of the same nature and was the result of hypertension, particularly since the albuminuria appeared to vary with the degree of hypertension and the most severe lesions were found in patients over 30.

Professor C. L. PIRANI (U.S.A.) demonstrated similar changes in the kidney in renal biopsies from 36 cases of moderate pre-eclampsia, but interpreted the glomerular intercapillary deposits as possibly new basement-membrane material, although there was no evidence of thickening or reduplication of the capillary basement membrane in cases of prolonged toxaemia and the staining reaction was not the same. Electron-microscopy studies of these cases revealed a glomerular lesion which appeared to be pathognomonic of pre-eclampsia. This consisted of swelling of endothelial and epithelial cells with deposition of new material, partly lipoid, in and between the cells. Unlike nephritic lesions there was no change in the epithelial foot processes and no proliferation of mesangium such as was suggested in a similar study reported by Professor F. TAKAKI (Japan). Repeat biopsies from these patients some months after delivery showed that the lesion was reversible. In a further study Professor PIRANI showed that the increase in blood uric acid varied directly with the severity of the renal lesions. Later in this session Professor EDITH POTTER (U.S.A.) referred from the chair to similar electron-microscopy studies by her colleagues Spargo, McCartney, and Winemiller which were in agreement with the findings of Professor Pirani and his associates.

Dr. H. B. GOODALL (Dundee) reported his study of haemoglobinuria in eclampsia. He confirmed Govan's finding a fibrinous vasculosis, and suggested that the haemorrhagic lesions in the liver were the cause of the haemoglobinuria.

Hypoxia of the Foetus

The meeting then passed on to consider the pathology of foetus and placenta. Dr. A. E. CLAIREAUX (London) summarized his findings in two surveys of perinatal deaths. One, a ten-year study, was carried out in Queen Charlotte's Hospital, London, and the other a study of all perinatal deaths in London and S.E. England during the nation-wide survey carried out by the National Birthday Trust in March of last year. He emphasized the very important part played by pre-eclampsia in causing stillbirth and neonatal death. The perinatal death-rate in conceptuses of toxaemic women was two and a half times the general level. All the evidence seemed to suggest that hypoxia of the foetus was one of the chief effects of toxaemia. His results showed the valuable nature of these studies, and the discussion of the pathological lesions indicated the great need for specialized training in this type of work.

Fibrinoid changes similar to those described in previous papers were demonstrated in a very convincing manner in the decidual arterioles of the toxaemic placental bed by Drs. H. G. DIXON and W. B. ROBERTSON (Jamaica). In a study of 200 biopsies they found the change developing within 10 days of the onset of pre-eclampsia, and suggested that this might be the cause of foetal anoxia. The conclusions drawn from the morning's meeting appeared to be that the lesions in most organs were clearly the result of hypertensive damage to vessels, and that this constituted the main danger to mother and child. In the case of the kidney a lesion pathognomonic of pre-eclampsia had been defined, but its pathogenesis still eluded us.

*Lendrum, E. C., *Proc. roy. Soc. Med.*, 1960, **53**, 338.

Salt and Water Metabolism

Much of the afternoon was devoted to the perplexing question of salt and water metabolism. Professor LÉON CHESLEY (U.S.A.) opened with a paper dealing with renal function and retrospective studies of salt metabolism. In pre-eclampsia there was a reduction of glomerular-filtration rate, he said, but the tubular reabsorptive capacity was increased and was geared to the prevailing glomerular-filtration rate. This would provide a reason for salt retention and oedema. Further studies in the puerperium showed that pre-eclamptic patients shed three times the weight lost by the normal pregnant woman and eight times the amount of sodium. These findings were in a sense at variance with those of Dr. I. MACGILLIVRAY (Aberdeen). Using heavy water and radioactive sodium and potassium, he made a careful study of normal and toxaemic primiparae under 30. The retention of water in normal pregnancy could be accounted for by the growth of uterus, breasts, foetus, placenta, the increase in plasma and red cells, and the liquor amnii. In pre-eclampsia these factors could not account for the greatly increased water retention. Sodium and chloride retention paralleled that of water in normal pregnancy, but in pre-eclampsia the exchangeable sodium and water remained the same as in normal subjects despite the increase of water.

Dr. D. A. DAVEY (London) added to our perplexity by serial studies of exchangeable sodium in 103 unselected primiparae, 11 of whom became toxaemic. In those patients who subsequently became toxaemic there was an excessive retention of sodium early in pregnancy, but when the toxaemia became overt the sodium content of the body rapidly fell. Dr. M. MAHRAN (Edinburgh), using tritium and radioactive sodium, produced results to show that water turnover was reduced by at least one-third in pre-eclampsia and exchangeable sodium was markedly increased. The position was summed up very well by Professor R. J. KELLAR (Edinburgh) at the end of the session when he said that much of the controversy might be related to the erroneous impressions gained by isolated estimations of these substances, and there was a need for serial studies in carefully selected substances.

Hormones, Enzymes, and Genetics

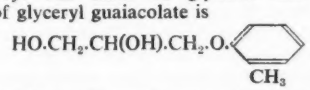
Two papers dealt with possible methods of estimating placental efficiency. Dr. A. KLOPPER (Aberdeen) reported studies of urinary oestriol excretion, which is diminished in pre-eclampsia. At present this method, while of considerable scientific interest, seemed of limited value in day-to-day changes of clinical state. Drs. M. J. R. DAWKINS and J. V. WIGGLESWORTH (London) presented a study of serum isocitric dehydrogenase, a water-soluble enzyme of placental origin. In severe pre-eclampsia this enzyme was greatly increased and appeared to be related to the formation of infarcts in the placenta. Professor LÉON CHESLEY (U.S.A.) reported a familial study which seemed to suggest that sisters and daughters of eclamptic patients were prone to develop pre-eclampsia, but Dr. EDDA HANINGTON (London) in a statistical study of blood groups could find no evidence of any genetic factor in pre-eclampsia. Professor M. MAGARA (Japan) presented his study of a water-soluble placental polypeptide vasopressor in nature, which bears a striking resemblance to posterior pituitary substance. A comparative study of pregnancy toxaemia in sheep by Dr. H. B. PARRY and Dr. HEATHER J. SHELLEY (Oxford) concluded the scientific contributions to this session.

To-day's Drugs

Glyceryl guaiacolate

"Robitussin" (A. H. Robins) contains 100 mg. glyceryl guaiacolate in each 5 ml.

Chemistry.—An ether of glycerol and guaiacol, the formula of glyceryl guaiacolate is



Pharmacology.—Glyceryl guaiacolate is an expectorant. Perry and Boyd[1] showed in rabbits that a dose of 0.01 g./kg. body weight given intraperitoneally increased respiratory-tract fluid by 185%. There have been no objective measurements of the volume or viscosity of sputum in man, the assessment of the drug being purely subjective. The evidence for the efficacy of this drug is, therefore, somewhat tenuous, but seems to indicate that its main effects are to reduce the tenaciousness of the sputum and diminish the frequency of coughing.[2] The latter effect is in part due to the demulcent action of the syrup used as a vehicle for the drug.

Therapy.—It can be used for the alleviation of all coughs, but more especially those associated with tenacious sputum. Dose: Adults—5–10 ml. (1 to 2 teaspoonsful) every 2–3 hours. Children—2–5 ml., 2 or more times daily, according to age.

Side-effects.—There appear to be no significant side-effects.

Contraindications.—Since the British preparation of robitussin contains no methylamphetamine, cardiovascular disease is no longer a contraindication to its use.

N.H.S. Basic Price.—8 fl. oz., 13s. 2d.

REFERENCES

1 Perry, W. F., and Boyd, E. M., *J. Pharmacol. exp. Ther.*, 1941, **73**, 65.
2 Hayes, E. W., and Jacobs, L. S., *Dis. Chest*, 1956, **30**, 441.

Framycetin

"Enterfram" (Genatosan).

Composition.—Framycetin is a wide-spectrum antibiotic, isolated in 1947 in France by Decaris from a strain of *Streptomyces lavendulae.* It much resembles neomycin both in its composition and in antibacterial action. Framycetin is not given systemically; its value lies in topical application; given orally it is poorly absorbed, being largely retained within the bowel. The preparation enterfram is a flavoured fluid for oral administration, containing 0.3 g. framycetin sulphate and 6.0 g. light kaolin (*B.P.*) in each 30 ml. (approximately 1 fl. oz.).

Antibacterial Activity.—Framycetin is both bactericidal and bacteriostatic; it is reported to be effective against most of the bacteria responsible for infective bowel disorders. These include many of the *Salmonella* group, including *Salm. typhi,* several serotypes of *Escherichia coli,* and all the species of *Shigella*; strains of *Staphylococcus* resistant to other antibiotics remain sensitive to framycetin.

Therapy.—Enterfram is intended for the treatment of most acute and chronic diarrhoeal disorders of infective bacterial origin; for the specific treatment of the bacillary dysenteries, of infantile diarrhoea and gastro-enteritis, and of acute bacterial food-poisoning. The advocated dosage for adults is 2 to 4 tablespoonfuls 6-hourly; that for children 2 to 4 teaspoonfuls, and for infants 1 to 2 teaspoonfuls similarly. A five-day course of treatment with framycetin generally has sufficed in acute infantile gastro-enteritis, the stools usually being freed from the causative *E. coli* within three days.

Side-effects.—Initial studies of framycetin showed its parenteral administration in some cases to result in severe kidney damage and injury to the eighth cranial nerve. It is therefore not advocated for systemic use. No evidence of these or other lesions has been reported as a result of its topical application or oral administration. No minor side-effects have attended its oral administration, and there are no recognized contraindications to giving it in this way.

N.H.S. Basic Price.—4 fl. oz., 11s.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

A Doctor's Duty

SIR,—At a time when the medical profession is becoming increasingly aware that the elderly respond remarkably well to adequate treatment and such treatment is being organized by geriatric units, many recently created, it seems unfortunate that the Bishop of Exeter (at the Annual Meeting of the B.M.A. at Torquay) should introduce a moral code designed to be particular to this age-group (see page 128).

It seems to me highly undesirable (and morally wrong basing the judgment on present practice) to bring a different standard of medical care to a patient on the grounds of increasing age and/or decreasing mental ability *per se.* At what age does old age begin? At what point of forgetfulness or dementia is an altered standard of care to be applied? Moreover, if dementia is cause for inadequate treatment, why not amentia? Again, at what price do necessary drugs become too expensive for this particular group of the community?

It is part of the normal practice of medicine to weigh the mental anguish and physical discomfort of the patient in relation to his treatment. It is also well recognized that at any age what is taken in the stride of one patient may be fearful and painful to another. Further, how define "extraordinary" means of treatment? In some patients mere movement in bed or a simple enema may cause more pain than an operation under anaesthesia or artificial feeding, although the latter sound more dramatic. The active decision not to use some "extraordinary" treatment is based on numerous clinical criteria, but the mere fact of being "over 65" or being unable to name the "Queen of England" seem odd weights to balance the scales. It should be remembered, too, that the penalties of inadequate treatment are not necessarily comfort and a quick death, but more likely to be thirst, pressure sores, parotitis, and incontinence.

A doctor is required to give adequate treatment to a patient from the time of birth to the time of death regardless of age or mental state. The medical decision that death will occur very soon, regardless of what is done, is an extremely difficult one to make at any stage, and particularly so in the elderly and at the point where "extraordinary" treatments, such as artificial feeding, are usually brought into use. The elderly become confused easily and uraemic easily and the resultant picture appears often hopeless when in fact it is not.

It cannot be too vigorously confirmed that we will continue our present code of conduct, that we do not believe in unnecessary suffering at any age, and that our diagnostic and therapeutic skill will be as richly adequate for second childhood as for first.—I am, etc.,

High Carley Hospital,
Near Ulverston. BRIAN LODGE.

Dental Extractions in Cardiac Patients

SIR,—Mr. H. McIntyre's article (June 11, p. 1778) is timely and valuable and is backed by the experience gained from the treatment of a considerable number of cases. In this hospital experience has led us to develop very similar procedures, but certain differences might be mentioned.

In discussing the indications for extraction I doubt if Mr. McIntyre is sufficiently radical. He uses the words "dental sepsis" and "infected teeth" without defining his standards.

In assessing the dividing line between conservation and extraction I think that there must be a swing towards a more radical treatment in all cases complicated by a heart lesion. This more radical approach is specially indicated in every proven case of subacute bacterial endocarditis, and I think that the work of Hobson and Juel-Jensen[1] might profitably have been mentioned in this connexion. They point out that cases infected with the *Streptococcus viridans* did not relapse after the mouth had been rendered edentulous. The advantages of extracting *all* the teeth in *every* such case must therefore be considered. In a letter to the *Lancet* (1956, **1**, 384) I have earlier stressed the role of dental sepsis in the aetiology of infection following operations on the heart. Many of these adult cases also are safer if rendered edentulous.

I have always given a longer period of penicillin cover than advocated by the author. It is known that 10 to 14 days elapse before epithelium covers a healing socket. I feel that the granulation tissue in the socket during this period is a ready means of ingress of organisms, especially during the early stages. I am specially concerned with the development of the dry socket, a percentage of which will occur in these cases, although the single injection of penicillin advocated may reduce the incidence. The continuance of penicillin cover not only helps to avoid this hazard but provides the opportunity for a follow-up brief inspection.

I am glad that Mr. McIntyre stresses that the use of adrenaline caused no complications in his series. I am quite sure that some vasoconstricting agent is required to ensure complete anaesthesia in dental extractions, in which diffusion of solution into bone is so important, and I have always preferred adrenaline to the other available analogues. I am surprised that the minimal amount of solution employed by him is 1.5 ml., for I find that 0.5 ml. or less is often sufficient. Dental injection cartridges contain 1.5 or 2 ml. of solution, and one finds this quantity routinely injected in both conservative and surgical work when much less will normally suffice. While his results showed no complications, I believe the minor disadvantages of local anaesthesia are less noticeable when less solution is employed.

While I appreciate that Mr. McIntyre is describing his proven techniques in a busy department, I wish he had reviewed the problem of anticoagulant therapy in his discussion. Experience shows that it is unnecessary to discontinue anticoagulant therapy during dental extractions so long as the prothrombin time is not more than twice the control figure. Even if patients are not receiving regular checks it seems advisable to determine the prothrombin time prior to surgery. A patient who has been led to appreciate the need for anticoagulant therapy is naturally apprehensive when it is discontinued. I think also it can be argued that it is illogical to stop treatment during a period of mental stress and surgical trauma.—I am, etc.,

St. George's Hospital, London, S.W.1. B. W. FICKLING.

REFERENCE

[1] Hobson, F. G., and Juel-Jensen, B. E., *Brit. med. J.*, 1956, **2**, 1501.

Hypothermic Coma in Myxoedema

SIR,—The problems in treating a comatose, or a myxoedematous, or a hypothermic patient are bad enough individually. I would like to congratulate Drs. J. H. Angel and L. Sash (June 18, p. 1855) on tackling them all together, and to add a few comments purely on the hypothermic part of the problem.

In general there are three ways in which a hypothermic patient can be brought back to normal temperature: very slowly by his own metabolism; by moderate warming as with blankets; or by rapid reheating—for instance, by immersion in a hot bath. As long ago as 1898 Sharpey-Schafer noted that patients who were not warmed at all after exposure seemed to do better than those who were, while since the last war a great deal of experimental and clinical evidence has been collected in favour of rapid rewarming. There are sound arguments in favour of both these methods, but very few would support what seems to be the common-sense way of moderate reheating.[1]

The intense peripheral vasoconstriction which follows cooling divides the body into two zones, a central core and a relatively avascular surface layer. The temperature of the surface layer drops far below the rectal temperature (which records the temperature of the core) an in fact approximates to the temperature of the environment. While the peripheral vasoconstriction remains, this intensely cold outer layer acts to a certain extent as an insulator protecting the core against further cooling. The only effect that moderate warming has is to open up the capillaries in this extremely cold tissue. When blood which has hitherto been safely confined to the core circulates through them the temperature of the core drops further (as recorded by rectal thermometer) and may cause death.[2] Very rapid rewarming is the direct answer to this problem. By this means, at the same time as peripheral capillaries open up the surface layers themselves are directly and immediately heated, and the core temperature does not drop.

Unfortunately, prolonged hypothermia is accompanied by a reduction in plasma volume and sudden vasodilatation may precipitate cardiac failure. A haematocrit estimation would reveal this state of affairs and then, of course, the best procedure would be to avoid peripheral vasodilatation altogether by allowing the patient to rewarm by his own metabolic processes. This is not achieved, as Drs. Angel and Sash suggested, by leaving the patient under a blanket, which would, in fact, produce peripheral vasodilatation, but by continued exposure. Talbott[1] estimated that to avoid peripheral vasodilatation the rectal temperature should not rise more than 1° F. per hour, and to keep it down to this rate may require additional cooling.

Myxoedematous hypothermia is a very complex situation and more must be known about the metabolic side before it can be said whether very slow or rapid reheating is most applicable. The cases quoted by Drs. Angel and Sash do not really help very much as far as treatment goes, because the two that died had core temperatures of 85° F. (29.5° C.), while the one that recovered had never fallen below 95° F. (35° C.). Howell[3] states that temperatures of 95° F. are not uncommon in patients over the age of 80 who are ill from any cause, and this patient was 82 and had carcinomatosis. In conclusion it might save a few lives to point out that cases of the more common condition of accidental hypothermia should never be treated by moderate rewarming.[4] Either very slow or very quick would do, but the latter is more convenient and immersion in hot water has the added advantage of providing hydrostatic support which reduces the demands made on the heart.—I am, etc.,

Lee-on-Solent, Hants. A. S. JARRETT.

REFERENCES

[1] Talbott, J. H., *Cold Injury*, 1951, p. 145. Macy Foundation, New York.
[2] Burton, A. C., and Edholm, O. G., *Man in a Cold Environment*, 1955. London.
[3] Howell, T. H., *Old Age*, 1944. London.
[4] Rees, J. R., *Lancet*, 1958, **1**, 556.

SIR,—On reading the article by Drs. J. H. Angel and L. Sash on myxoedematous coma (June 18, p. 1855), I felt that the following case should be recorded.

During the winter of 1949 I was asked, while visiting a patient, to "take a look at her sister" who seemed to have "slowed down." This lady was on a Christmas visit, had

not seen her sister for some months. I saw a small countrywoman, with wiry iron-grey hair, thick eyebrows, tanned skin, and a bright colour. I detected nothing unusual on physical examination, except a blood pressure of 180/90. She said she felt "quite well."

Two weeks later, in very cold weather, during a severe influenza epidemic, I was called to the house because they could not wake her after a night's sleep. She was 64 years of age. On examining her, pupils were equal, reflexes all normal. She was deeply unconscious, with stertorous breathing. I failed to get an immediate hospital bed, so I moved her to a near-by nursing-home. A catheter produced no urine, so diuresis was induced (I was besotted by idea of diabetic coma), and a perfectly normal urine, about 5 oz., passed. I was ignorant of thyroxine, but the nurse had found that by placing a spoonful of liquid at the back of her tongue, and holding her jaw, she could be induced to swallow. We ground up 5 gr. (0.32 g.) of thyroid (*B.P.*) tablets in a teaspoon of water, and placed it on her tongue. Four hours later she was conscious, but disorientated. This cleared in 24 hours, and she has never looked back. She takes a maintenance dose of thyroid, 1½ gr. (0.1 g.) daily.

The diagnosis was by elimination. I could think of nothing else that would fit the case, and felt a therapeutic trial justified. On reading the literature I realized how grossly I had erred, and how lucky a G.P. may be.—I am, etc.,

Birkenhead. GRACE BOWEN.

SIR,—I have read with interest the paper by Drs. J. H. Angel and L. Sash (June 18, p. 1855). Under the heading "Other Measures" there is a short note on artificial ventilation. Carbon-dioxide narcosis is believed by Nordqvist *et al.* (personal communication) to be the cause of coma, both their cases regaining consciousness *within ten minutes* of the commencement of artificial ventilation, although treatment with a respirator was required for a further two weeks. The importance of this finding must be stressed. I would suggest that artificial ventilation be considered an immediate emergency measure in the treatment of such cases. —I am, etc.,

Cleveleys, Lancs. D. W. MACDONALD.

Reaction after Saccharated Iron

SIR,—On May 9 I gave an expectant mother her second injection of "ferrivenin" (saccharated iron oxide) 5 ml. of Batch 3995. Five minutes later she had a severe anaphylactoid reaction with bronchospasm, restlessness, vomiting, swelling of tongue (subjective), and later urticaria. About 15 minutes after 0.5 ml. adrenaline she improved, and the foetal heart did not seem to be affected. The next day another expectant mother had the same reactions following 2 ml. of the same batch given as the third dose. On this occasion the patient complained of running of eyes and nose, and had her bowels open as well. There was a history of hay fever in this case.

I had previously given to other patients one ampoule (5 ml.) of this batch without ill effects, and have given other batches before and since without ill effects. Messrs. Benger Laboratories Ltd. have since retested samples of Batch 3995 and found no abnormal toxicity. It would be interesting to know if allergic reactions have been previously noted associated with the use of this usually non-toxic drug.—I am, etc.,

London, N.8. J. DAFF.

"Phisohex"

SIR,—In discussing the use of "phisohex" for the surgical scrub, Mr. V. J. Kinsella (December 19, 1959, p. 1402) has drawn attention to the different conclusions reached by Smylie *et al.*[1] and Göpel *et al.*[2] Mr. Kinsella has suggested that in the method used by Smylie *et al.* to evaluate the bactericidal effect of phisohex there may have been insufficient contact between phisohex and the antagonizer, "tween 80." In view of this it is felt that the procedure used in this laboratory and the results obtained will be of interest.

We were interested in the relative effectiveness of phisohex and a 2% hexachlorophene soap. Previously surgeons in this hospital carried out a five-minute scrub with hexachlorophene soap. Phisohex was used according to the manufacturer's directions, i.e., a preliminary wash followed by a four-minute scrub. A series of swabs were taken after surgeons had scrubbed with hexachlorophene soap and after surgeons had scrubbed with phisohex. In each case pre-operative swabs were taken before the surgeon donned gloves and post-operative swabs immediately after the surgeon removed his gloves. A swab was moistened with nutrient broth containing 1% tween 80, rubbed along the fingers and side of the surgeon's hand, and placed in the same broth. After overnight incubation at 37° C. the broths were plated on blood agar. Broths showing growth were regarded as positive.

To determine whether 1% tween 80 would be a satisfactory antagonizer, the following experiments were carried out:

1. The level of phisohex antagonized by 1% tween 80 was determined. Twofold dilutions of phisohex were prepared in nutrient broth and in nutrient broth containing 1% tween 80. Both series were inoculated with *Staphylococcus aureus*, incubated overnight at 37° C., and plated on nutrient agar. Growth in the two series was compared

Inoculum		Phisohex Dilution Showing Growth	
Strain	No. of Organisms per ml. of Broth	Nutrient Broth Containing 1% Tween 80	Nutrient Broth
Phage type 80 81 strain (1)	20,000	1:800	$1:8\times10^6$
,, ,, 80 81 ,, (2)	600	1:512	$1:2\times10^6$
,, ,, 80 81 ,, (3)	100	1:1,024	$1:5\times10^6$
	1,000	1:512	$1:2{\cdot}5\times10^5$
	10,000	1:512	$1:2{\cdot}5\times10^5$
,, ,, Group II	20	1:256	$1:5\times10^5$

(see Table). The number of organisms in the inoculum used was estimated by the method of Miles and Misra.[3] It can be seen that 1% tween 80 permitted even the most sensitive strains of staphylococci tested to grow in a phisohex concentration of 1:1,000. There is a considerable margin between this and the level of phisohex likely to be present on a swab (see below).

2. It was shown by the use of Miles and Misra counts that 1% tween 80 has no inhibitory effect on *Staph. aureus*.

3. The amount of phisohex likely to be present on a swab taken after a phisohex scrub was estimated. Hand swabs were taken after a surgical scrub with phisohex and placed in nutrient broth. A series of dilutions of this broth was then compared with a series of dilutions of phisohex. Thus we had two series of broths: a test series containing unknown concentrations of phisohex and a standard series containing known concentrations of phisohex. Both series were inoculated with a standard suspension of *Staphylococcus aureus* phage type 80/81. After overnight incubation at 37° C. the broths were plated on nutrient agar. The above procedure was carried out on ten swabs. By comparing the dilutions of broth and phisohex in which growth occurred, it was shown that the concentration of phisohex present in the broth from scrubbed hands was less than 1:200,000.

Results

Swabs were taken from ten surgeons. Twenty-eight swabs were taken after hexachlorophene soap scrub of which 25, i.e., 89%, were positive, and 25 post-operative swabs were taken of which 23, i.e., 92%, were positive. After phisohex scrub, 30 pre-operative swabs were taken of which 3, i.e., 10%, were positive, and 30 post-operative swabs were taken of which 2, i.e., 6.7%, were positive.

It is felt that this method of testing overcomes the objections raised to the work of Smylie *et al.*, since in a liquid medium there would be more intimate contact between phisohex and antagonizer. The transfer of phisohex-treated organisms to broth containing antagonizer approximates more nearly to the situation which arises when such organisms are exposed to blood or serum. The results obtained support the conclusion that the use of phisohex for the surgical scrub results in a considerable reduction in the number of organisms present on the skin.—I am, etc.,

Palmerston North Hospital, New Zealand. AUDREY W. JARVIS.

REFERENCES

[1] Smylie, H. G., Webster, C. U., and Bruce, M. L., *Brit. med. J.*, 1959, **2**, 606.
[2] Göpel, H., Rücker, R., and Schütz, W., *Chirurg.*, 1958, **29**, 433; 1959, **30**, 116.
[3] Miles, A. A., and Misra, S. S., *J. Hyg. (Lond.)*, 1938, **38**, 732.

Appendicitis in Pregnancy

SIR,—Mr. W. P. Black is to be congratulated upon his article on "Acute Appendicitis in Pregnancy" (June 25, p. 1938), in particular for stressing the importance and difficulty of early diagnosis.

I write to add two points which may be of value. First, the tongue. The brown, furred, rather dry tongue of the acute appendix may be diagnostic. The second concerns the differential diagnosis between acute appendicitis and unilateral right-sided pyelitis, in which, during the first 48 hours, he rightly states the urine obtained by catheterization of the bladder may be sterile. Instead of awaiting the effect of postural treatment, I suggest that immediate cystoscopy will show whether or not the urine in the bladder is coming from both ureters or only the left.—I am, etc.,

London, W.1. J. D. FLEW.

Oral Diuretics in Pregnancy Toxaemia

SIR,—I was interested in the letter of Drs. John D. Watt and Elliot E. Philipp (June 11, p. 1807) reporting five cases of intrauterine foetal death in mothers with pre-eclampsia treated with oral diuretics and in their suggestion that the use of diuretics, though effective in removing fluid and lowering blood-pressure, may have contributed towards the foetal loss by masking the true state of the disease.

A clinical evaluation of three diuretics—"hydrenox" (hydroflumethiazide), "saluric" (chlorothiazide), and "hydrosaluric" (hydrochlorothiazide) (usual dose hydrenox 50 mg. twice a day or equivalent)—has been made at the Nottingham Hospital for Women during the last 12 months. It is hoped to publish the results at a later date. Compared with cases treated by rest and sedation alone, an impressive diuresis has been obtained in many cases admitted with the full signs of pre-eclampsia or with hypertension only, but the response is unpredictable and poor in as many as 25%. Cases of pre-eclampsia with quite marked oedema do not appear to have any better diuresis than those with hypertension alone. There has been little fall in blood-pressure over and above that which would probably have been achieved by rest and sedation. The degree of reversal in the signs of pre-eclampsia seems often unrelated to the diuresis obtained, and is again probably little different from that achieved by bed rest and sedation alone. Thus the action of the diuretic is to relieve one of the important effects of pre-eclampsia without influencing the cause, and its place should be regarded as that of a useful addition to present-day therapy rather than a substitute for it.

With regard to intrauterine foetal death, it must be remembered that placental insufficiency may be due to changes in the placenta developing over the course of some weeks prior to the appearance of pre-eclampsia in the mother, and improvement in foetal survival in hypertensive toxaemia of pregnancy awaits a simple, quick, reliable method of assessing placental function. In the 126 cases studied, there have been only two stillbirths; both were intrauterine foetal deaths. One was a case of eclampsia in which the baby died 12 hours after admission; the other was admitted with a blood-pressure of 200/120, having had an accidental antepartum haemorrhage at 30 weeks' gestation. Intrauterine foetal death occurred three days after admission.—I am, etc.,

The Nottingham Hospital for Women, Nottingham. R. T. SEARS.

Delay in the Third Stage

SIR,—I have been very interested in reading the correspondence on the Brandt–Andrews method of delivery of placenta. I introduced this technique in the Peterborough Group of Hospitals in July, 1954,[1] and it has been in continuous use since that date. The results of the use of this technique up to the end of 1958 have been recorded in the *Proceedings of the Royal Society of Medicine*.[2]

It might be of some interest to those who are contemplating using the Brandt–Andrews technique to know that nine midwives using this method over the period 1957–8 in my obstetric unit in 1,349 consecutive deliveries had the following results: fundal pressure was used in 85 patients with five cases of post-partum haemorrhage, and in 1,264 patients the Brandt–Andrews technique was used with eleven cases of post-partum haemorrhage. The average blood loss, excluding the post-partum haemorrhage, was 3 oz. (85 ml.); the average time of stage III was four minutes, excluding cases of manual removal. Manual removal was necessary in thirteen cases (1%). The technique is easy to perform, but those who have not done it before should apply gentle sustained cord traction at first, and as experience grows the correct amount of tension on the cord will be more readily assessed.

The Brandt–Andrews technique has now been used in many thousands of patients in the obstetric unit in this group of hospitals, and we are teaching this method to students who come to us for one month's midwifery training from one of the well-known London teaching hospitals. I think it would be unwise for the Brandt–Andrews method to be used if ergometrine (0.5 mg.) is not given either intravenously with the delivery of the anterior shoulder, or 0.5 mg. ergometrine intramuscularly with hyaluronidase as soon as the head is crowned.[3]—I am, etc.,

Peterborough. NORMAN KIMBELL.

REFERENCES

[1] *Brit. med. J.*, 1958, **2**, 155.
[2] Kimbell, N., *Proc. roy. Soc. Med.*, 1959, **52**, 569.
[3] —— *Brit. med. J.*, 1954, **2**, 130.

Vacuum Extractor in Obstetrics

SIR,—I have been interested at the observations of Dr. James Willocks (June 18, p. 1886) on the use of the "ventouse" at Glasgow Royal Maternity Hospital, and have had an opportunity of discussing this with Professor Ian Donald. Although in the Glasgow series failure with the ventouse has been commoner than it has here, there are two possible explanations. Firstly, Glasgow has always had a bad reputation for pelvic deformity, and I think it probable that cephalo-pelvic disproportion, in which detachment of the ventouse often occurs, is commoner there than in most centres. The fact that one case was eventually delivered by caesarean section seems to confirm this. Secondly, we have found here that greater experience of the method has led to improvement both in technique and in our selection of cases for vacuum extraction, so that recently failure has become very rare, and I hope that further experience with the ventouse, which Dr. Willocks mentions, will lead to better results in Glasgow.

The experimental use of the vacuum extractor in the stillborn foetus may be misleading, in that the formation of the chignon is to some extent due to the obstruction of the venous return from the relevant area of the scalp by the pressure of the rim of the cup during induction of the vacuum. The figures given by Dr. Willocks are not in agreement with those of Rosa,[1] who has calculated that it is possible to exert a pull of almost 30 kg. (65 lb.) without detachment.

With regard to Case 87, we have quoted this as an extreme example of the range of the method and agree that caesarean section would have offered as safe a method of delivery in this case. None the less, in a woman who has had three normal deliveries, the urge to avoid section is strong. In a later paper,[2] however, read at the Royal Society of Medicine, I have stated, "Such a case is usually better dealt with by caesarean section, and only when the cervix is three-quarters or more dilated should the ventouse be employed."

Like the writer, we have found it impossible to replace forceps completely with the ventouse, but we feel that the latter is, in the absence of disproportion, the ideal instrument for the case in which delivery is indicated when the head is arrested in mid-cavity with the occiput either posterior or lateral (as it is in most cases where the indications for mid-forceps delivery are present). In these circumstances the ventouse imposes materially less trauma on the child than does a mid-forceps operation with either manual or forceps rotation as opposed to the "auto-rotation" which we have found such a satisfactory feature of the ventouse. In our second paper quoted above we have stressed the use of the ventouse in cases requiring rotation and in malpresentations, and we feel that ultimately these and cases of delay in the late first stage will constitute the field in which we find the greatest usefulness of the ventouse rather than those in which simple forceps is the alternative.—I am, etc.,

Ronkswood Hospital, Worcester. J. A. CHALMERS.

REFERENCES

[1] Rosa, P., *Bull. Soc. roy. belge Gynéc. Obstét.*, 1955, **25**, 142.
[2] Chalmers, J. A., *Proc. roy. Soc. Med.*, 1960. In press.

Laissez-faire Antenatal Care

SIR,—Dr. Hamish G. Nicol (May 14, p. 1504) put up a plaintive protest about inadequate antenatal care afforded to three of his patients before their transfer to the care of his practice. I have watched for any published reply to his restrained and reasonable query, but with the exception of Dr. Heber's letter (May 28, p. 1658) no one else seems interested. Are we to assume that the doctors attending these three patients are the only ones who failed to deal with anaemia in pregnancy: or, as both Dr. Nicol and Dr. Heber hold the D.Obst.R.C.O.G., have we here support for the view held by at least some obstetric committees that those who wish to add their names to the local obstetric list should have had postgraduate training in obstetrics? Can we not hear from some of the gentlemen who vociferously insist that the local obstetric lists should indicate merely those willing to carry on obstetrics rather than those possessing skill and experience in the art?—I am, etc.,

Health Department, County Hall, Lewes. F. LANGFORD.

Premedication

SIR,—May I offer a brief comment on the letter from Dr. T. W. Baillie (June 18, p. 1886) regarding premedication for operative obstetric procedures? At the Second World Congress of Anaesthesiologists in Toronto next September I shall be presenting evidence that promethazine ("phenergan"), given intravenously to the mother, begins to reach the foetus within one or two minutes, as Professor William W. Mushin (May 21, p. 1558) indicated. The concentration in the foetal blood will certainly rise to significant levels after a 50 mg. dose. My paper will, I think, convince Dr. Baillie. I feel impelled to write this warning note because I think that Dr. Baillie is in danger of falling into the very trap which I myself stupidly entered a couple of years ago—that of accepting uncritically a "work in progress" note as adequate support for one's entrenched clinical impressions.

Working at the Columbia-Presbyterian Hospital, New York, last year, in Dr. Duncan A. Holaday's laboratory, and with the encouragement and assistance of Wyeth Laboratories (the manufacturers of phenergan in the United States), I soon found that the original method of assay of the drug in blood, as used by Adelman *et al.*,[1] was unsatisfactory. The method which was finally evolved, when applied to clinical material, led to the conclusions I have stated. A discussion of the clinical implications of these facts, though included in my paper, would be out of place in this letter.—I am, etc.,

London, N.W.3. J. SELWYN CRAWFORD.

REFERENCE

[1] Adelman, M. H., Fisch, H., Jacobson, E., and Katz, J., *Anesthesiology*, 1958, **19**, 93.

Prolonged Survival of Bone-marrow Graft

SIR,—With reference to the remarkable article "Prolonged survival of a bone-marrow graft, etc.," by Dr. J. O. W. Beilby *et al.* (January 9, p. 96), the following observation may be of interest.

A woman, now aged 39, suffering since 1950 from (secondary) thrombocytopenic purpura was splenectomized in 1955. Two years later a marked bleeding tendency developed, becoming progressively worse. The patient had extensive purpuric and ecchymotic skin manifestations, frequent haemorrhages from the nose and mouth, and profuse menorrhagia; the number of platelets decreased to very low figures. Continuous treatment with blood transfusions and steroids in high doses was of no avail. As the haemorrhagic tendency became uncontrollable, I decided to try homotransplantation of bone-marrow. Three such

attempts were made, two in 1957, one in 1958. For the first and second transfer the husband (aged 37) and brother (aged 39), respectively, served as marrow donors. Sternal marrow, 4–6 ml., aspirated with siliconized instruments was directly (within less than one minute) injected into one iliac marrow cavity of the patient. Both implantations had no effect on the platelet count or the bleeding tendency. Consequently, treatment with blood transfusions and steroids was resumed, again without any favourable influence on the clinical picture and the platelet count.

About one year later (July, 1958), with a platelet count of 10,000, the third trial with intramedullary implantation of homologous bone-marrow was made. The technique was the same as in the previous procedures. Donor was this time a *sister* of the patient (aged 34). 4 ml. of her sternal marrow was directly injected into one iliac bone-marrow cavity of the patient. Following this marrow transfer the bleeding tendency improved gradually and the platelets increased to 45,000 during the next four months. In January, 1959, the count had reached 110,000, and the level has been maintained ever since between this figure and the minimum of 83,000 platelets/c.mm. The patient has been free of bleeding manifestations except occasionally for small ecchymoses on her legs (particularly premenstrually). The sternal marrow, re-examined in May this year, contained a number of megakaryocytes, part of these of the platelet-forming type. These findings are in contrast to numerous previous marrow examinations (prior to the marrow implantation in July, 1958), when megakaryocytes were absent.

The course of this case, which will soon be published completely, favours the concept that homologous bone-marrow implantation in man is not valueless in principle. The following prerequisites appear important: (1) close relationship (same sex) between donor and recipient, and (2) direct transfer of the marrow aspirate to the patient without delay. Dr. Beilby *et al.* have attributed their success with bone-marrow graft to similar factors. As to the mode of administration, for various reasons intramedullary implantation of the donor marrow seems to me preferable to intravenous injection.—I am, etc.,

New York 21, New York. GEORGE ROSENOW.

Eradication of Malaria

SIR,—Dr. R. B. Heisch is quite correct in pointing out in his letter (June 4, p. 1736) that your leading article entitled "Eradication of Malaria" (April 2, p. 1033) underestimated the amount of work carried out during the past few years in Africa with the aim of malaria eradication. Since 1955 much effort was devoted to this task by a number of countries and territories in Africa, increasingly assisted by the World Health Organization. At the end of 1959 there were in Africa ten malaria eradication pilot projects in progress, stimulated and helped by the World Health Organization. Four of them (Liberia, former French Cameroons, Uganda, and Southern Rhodesia) produced very encouraging results. A large malaria eradication programme covering several countries or territories of South-East Africa is in a preliminary stage. A detailed report on the present situation and an outline of future work in Africa were presented by W.H.O. to the Thirteenth World Health Assembly in May, 1960.

Dr. Heisch is less justified when he states, rather dogmatically, that malaria eradication in Africa should be carried out through the administration of antimalarial drugs alone. It is true that in a number of pilot projects in tropical Africa there were some difficulties of the "complete coverage" by residual insecticides and the results were disappointing. Some difficulties were due to operational and administrative shortcomings, others due to technical problems. Nevertheless, it seems that where the application of residual insecticides was properly carried out the results were promising.

Although the value of antimalarials as an adjuvant method of malaria eradication has been fully recognized it would be overoptimistic and unjustified to rely for malaria eradication on chemotherapy alone. Regular, repetitive, mass treatment of an entire population can seldom (if ever) be carried out for any length of time until we develop a drug with a long-lasting effect which can be administered by a single dose at widely spaced intervals. In order to assess the value of mass administration of antimalarials and the operational problems connected with it a number of field trials are now in progress in several African areas. One of these trials aims at assessing the value of medicated salt according to Pinotti's method and is in its early stage in West Africa. The present consensus of the opinion is that antimalarial drugs have an important part to play in malaria eradication, especially in the later stage of the programme. In the early stage the drugs might be used as an *additional* measure only where residual spraying was not fully effective in interrupting the transmission of malaria or where the imagocidal measures were unduly slow.

Many arguments could be brought up against Dr. Heisch's proposed use of the "sporozoite rate" as a more sensitive index of transmission than the parasite rate. A discussion on this rather special subject in a general medical journal would be out of place, but suffice it to state that all the practical epidemiological experience points to the fact that the "sporozoite rate" is not a sensitive index of malaria transmission since its significance varies greatly, not only in relation to seasons, breeding activity of *Anopheles*, their mean age, but also to the numbers of dissected females in each area and the time between their capture and their dissection. Moreover, in some areas *Anopheles* carry the sporozoites of non-human malaria which may confuse the conclusions. The infant parasite-rate is probably a more sensitive index of transmission of the disease before the case detection of individual infections can be instituted.—I am, etc.,

Geneva. L. J. BRUCE-CHWATT,
Chief, Planning Division of Malaria Eradication, World Health Organization.

Treatment of Bacillary Dysentery

SIR,—In studying the article by Dr. A. R. D. Adams (May 28, p. 1639) it would appear from the variety of drugs referred to that no one of them is specific in getting rid of the infecting organism.

Sonne dysentery, as at present encountered in my district, is a mild disease and some general practitioners are of the opinion that it is wasteful to use the antibiotics in treatment. This opinion may be justified if the object of treatment is simply to deal with the symptoms. I believe that, for the effective treatment of dysentery, one must consider not only the symptoms but also the subsequent carrier state. I would like to know if there is any evidence to support the view that a full course of antibiotic drugs as suggested does in any way reduce the carrier rate after treatment.

The Public Health Laboratory will, on request, carry out sensitivity tests on the organism isolated. Will the use of drugs to which the organism is sensitive really reduce the carrier rate or cut down the period for which persons may be carriers? What treatment does the

author recommend to get rid of the carrier state (*a*) after an acute attack of the illness, (*b*) ascertained in the course of routine investigations? The exclusion of children from school is an unsatisfactory method of dealing with the problem, whilst the risk of handlers of food or drink becoming infected (or becoming carriers) has become increasingly obvious to me. The main holiday season is approaching: What advice should one give to parents with "carrier" children in the family, bearing in mind that there are many other carriers one knows nothing about?—I am, etc.,

Dereham, Norfolk. A. B. GUILD.

Diarrhoeal Diseases

SIR,—Dr. H. Cairns (June 25, p. 1954) has hit the nail on the head. The importance of clean hands when handling food is ignored. I have never seen my mother or her sisters ever start preparing food without washing their hands first. They are all around 70 years of age, and were brought up to regard clean hands as vital. It is fantastic that, with the so-called improved standard of living, houses are still being built with lavatories with no wash-basin in the same room. Many small restaurants provide no washing facilities for patrons. Even when cloakrooms are provided—often most luxurious—the washing facilities are ignored. Tremendous care may be taken with hair and make-up, but so often the hands are not washed.

Even in fashionable girls' schools no instruction is given on this subject, and, unless instruction has been given at home, a high standard of knowledge may be gained without even an elementary knowledge of hygiene. It is rare to find either soap or a towel in a cinema cloakroom, yet even British Railways provide these. I understand that some London boroughs provide liquid soap and paper towels free. As for "sink tidies," yesterday's newspaper and a kitchen bin completely obviate the need for this abomination.—I am, etc.,

London, W.2. MARGARET JOAD.

High-pressure Salesmanship

SIR,—Dr. J. Bunting suggests (June 4, p. 1741) that, from the viewpoint of a manufacturer of a new drug, it is "enough to announce and repeat the fact in . . . professional periodicals." He says that really effective market research consists in "using one's own good common sense," and that he knows for a fact that medical journals "are read through from cover to cover by a large percentage of practitioners." "Large percentage" means presumably at least 75%. If so, I fear Dr. Bunting's good common sense has led him badly astray. Market research has long ago revealed the fact that the readership of medical journals is much less than one might imagine; though obviously I had better not attempt to quote comparative figures here. Circulation is not the same as readership; and readership is certainly not the same as "cover to cover" readership. Indeed, you, Sir, are quoted in the same issue of the *Journal* (p. 1731) as saying of it that it was "unlikely that anyone would read the whole of a particular issue." Of course, there are exceptions. Most journals very properly charge extra for advertisements in special positions (e.g., facing reading matter), for such advertisements are thought more likely to be read.

The sales director of any ethical pharmaceutical firm would accept that, for nine out of ten new drugs, if he had to choose between using advertisements or using mailings, he would use mailings every time; and he would add that, if he wished the drug to have a chance of wide usage, he would send out repeated mailings. Indeed, the wonder to me is that any firm should insert an advertisement in the solid advertising section of a medical journal. A statement in such an advertisement to the effect that a sample of a drug is available will bring in a handful of requests: a similar statement in a mailing to all general practitioners will bring in two to three thousand requests on average. These are facts, whatever common sense might suggest.

It is, of course, irritating to have eight or ten mailings through one's letter-box every morning; but irritation is no bar to receptivity, and no one would be more pleased than the harassed manufacturer if an alternative way were devised of quickly informing a majority of doctors of at least the name of a drug and its indications and advantages. Indeed, I would guess that the public relations efforts of certain manufacturers—efforts recently under fire in the *Journal*—were *au fond* hopeful attempts to meet the repeated criticisms of the welter of mailings we all receive. Any doctor who has ideas for a worth-while and economical alternative to the welter should get in touch with the nearest pharmaceutical firm. He will shortly find himself on its board. Incidentally, every cloud, etc.: if, like me, one has a number of small children, the envelopes in which pharmaceutical mailings come will be found most useful for scribbling and drawing space missiles on, and for playing at postmen with.

Perhaps I should add that I work in the pharmaceutical industry and that I am not a masochist.—I am, etc.,

Amersham, Bucks. S. BRADSHAW,
Medical Consultant,
Aspro-Nicholas, Ltd

*** In a careful statistical survey published in 1958 (*Brit. med. J.*, **2**, 1096) Dr. Audrey Z. Baker found "a *British Medical Journal* readership of between 80% and 90% throughout all areas" of the United Kingdom.—ED., *B.M.J.*

SIR,—The pharmaceutical firms' circulars have long presented a difficulty to us. We gave up reading them many years ago, when it had obviously become impossible to evaluate their contents. Now the difficulty is to separate them from the other mail and to dispose of them as quickly as possible. At the same time they represent an appalling waste of money.

During a recent single week we received 43 circulars for my wife and 13 for myself. I cannot guess what it costs to produce each of them. An estimate of 1s., including the stamp, appears conservative. If, for simplicity's sake, we estimate that 20,000 general practitioners receive 43 circulars each every week and 20,000 other doctors 13 each, then the yearly sum spent on this amount of advertising works out at £2,912,000. If we realize that a great deal of this money derives from drugs sold under the National Health Service, we must come to the conclusion that we could have had a new general hospital or ten new health centres for general practitioners every year instead of these circulars. We know these firms are doing their best to tell us all about their new products. Perhaps the main fault lies with the tax system which allows tax relief on advertising. I do not know the answer to this problem. One thing that might help would be if all the drug firms agreed to combine in one monthly review only, carrying all their separate advertisements. This might perhaps contain some original articles, reporting objectively on new products.—I am, etc.,

Leigh, Lancs. F. R. ZADIK.

Locked Twins

SIR,—In the *Journal* of April 16, articles on locked twins by Dr. S. K. el Deiry (p. 1174) and by Mr. I. J. Cunningham (p. 1184) stress the rarity of this condition. We have had two similar cases here during the past 16 years.

One was in Blantyre Mission Hospital (now closed), where we were responsible for 24,060 deliveries in hospital and district centres during that time, abnormal cases being sent to hospital. The incidence of twins is about 1 in 35 here, so there would be about 680 twin deliveries. The patient was a young primigravida who was admitted after some time in the second stage of labour. On examination both bags of membranes had broken; the leg and cord of one child and the head of the other were all in the vagina. Under general anaesthesia it was possible to replace the leg in the uterus and deliver the vertex presentation (which was alive) by forceps, and then to do a breech extraction of the other child, which had been dead some time.

The other case was in Mlanje, where during the past 16 years we have supervised 16,165 deliveries in hospital and district—i.e., about 460 cases of twins. The patient was a multipara-10 who had had twins once before. She was admitted after two days' labour in the village, fully dilated, both bags of membranes having broken, with the arm of one child and the head of the other in the vagina. The arm was replaced in the uterus, and the vertex presentation delivered spontaneously an hour later, when the arm again prolapsed as the second twin was lying transversely. An internal version and breech extraction was done. Both babies were alive and weighed 6 lb. 7 oz. (2.92 kg.) and 5 lb. 12 oz. (2.51 kg.)—the average birth weight for single babies is 6 lb. 7 oz. (2.92 kg.) here.

It is surprising that this complication does not occur more often in this country, as twins are common, and women in the villages are made to push from the first contraction during labour, with resultant early rupture of membranes.—I am, etc.,

The Mission Hospital, Mlanje, Nyasaland. R. GWEN DABB.

Conjoined Twins

SIR,—The following case of conjoined twins illustrates the fact that even *x*-rays in pregnancy may not eradicate all problems.

Our patient was a five-para who was admitted in labour without having attended the antenatal clinic. She was examined by the doctor on duty, who diagnosed twins. The cervix was about three-fingers dilated and a small head was presenting, but the position of the second twin could not be defined, as the abdomen was somewhat tense.

By the morning the head had reached the perineum but progress was slow. With difficulty the head and shoulders were delivered, but there the child stuck. The patient was given an anaesthetic and a hand passed into the uterus. A hand was encountered, and at first it was thought that the twins were locked, but when the hand was followed to the shoulder it was found that this apparently was attached to the chest of the first child. A diagnosis of conjoined twins was made, and the patient taken to the theatre, where a caesarean section was performed. The babies were attached by the thoraces and had to be separated, one being delivered through the abdominal wound and the other through the vagina. The children, females, had one placenta, one heart, and one liver.

It was only on the third day after delivery that the patient told us that she had been to another hospital previously and had had an *x*-ray. She was told that there were two babies, and that she ought to be in hospital for her delivery. There seems to have been no suggestion that there was any abnormality.—I am, etc.,

Mure Hospital, Nagpur, India. M. A. HARVIE.

Is Trichomonal Infestation Venereal?

SIR,—Commenting on the letters by Dr. L. Watt and Professor H. C. McLaren (May 14, pp. 1502 and 1503), Dr. C. S. Nicol (May 28, p. 1654) has underlined the important point about the diagnosis and treatment of disorders which, though venereal in origin, do not presuppose necessarily that the persons involved are sexually promiscuous. With so much of the work in many of the special clinics involving lower genito-urinary disorder (often with complications) in married couples who have not recently been sexually promiscuous, it is important that they should be able to attend special clinics without that attitude of mind engendered in the past by the phrase "V.D."

As Dr. Nicol points out, attitudes are changing, and many practitioners to-day avail themselves of the facilities of these clinics for the investigation of this sort of patient. Provided the phrase "V.D." is left out of the conversation, there is never any difficulty with this work, and I doubt whether the inception of yet another clinic in the hospital would further the interests of the patient. Also one cannot help thinking that the very special alarm aroused by the title "Venereal Disease Clinic" will become less general in future as enlightenment spreads.—I am, etc.,

Guy's Hospital, London, S.E.1. A. S. GRIMBLE.

Survival in Nuclear War

SIR,—No one could read Dr. Arthur Speight's letter (June 11, p. 1809) without sympathizing with his point of view. There are, however, certain facts that should be considered. In this century that has originated genocide, can we be sure that the loser will only have to live under a hated totalitarian regime? Is it to be supposed that a great nation will submit to defeat whilst only using conventional weapons?

Some 700 years ago St. Francis said, "You can always have peace if you will give up your possessions." It would mean all our luxuries and probably some of our necessities. Although perhaps a surprising number of people would agree to do this and even risk martyrdom rather than unleash this horrible weapon, I am afraid that they are only a very small minority.—I am, etc.,

Penzance. D. C. CLARK.

"Honour a Physician"

SIR,—Your reviewer, Professor D. V. Hubble, must surely have lost all sense of humour when he read *Honour a Physician*, for his comments on Philip Auld's book (May 28, p. 1625) are most misleading and unjust. I know a large number of people who have been greatly entertained and who have enjoyed many a good laugh out of this extremely well-written novel. The author makes it perfectly plain that it is a minority of patients and doctors who create the problems he refers to. He also shows, very convincingly, how a keen and hard-working young doctor, with great initial enthusiasm for the Health Service, gradually becomes disillusioned and frustrated in his attempts to educate the public and to inculcate a sense of personal responsibility.

Philip Auld's work is both a very humorous and a very serious book. Much of the dialogue is brilliant

and echoes situations similar to many I have experienced or heard of from general-practitioner colleagues. Professor Hubble is surely wrong in implying that such problems as exist are confined to industrial areas, for I find variations on the same theme in central London, its suburbs, and the surrounding country. *Honour a Physician* is an outstanding psychological and sociological study which deserves to be read by everyone who has the true interests of medicine at heart.—I am, etc.,

Radlett, Herts. REGINALD S. MURLEY.

SIR,—Surely there are many, many G.P.s who would support "Unhonoured" (June 18, p. 1892) in his protest against your reviewer's criticism of this book (May 28, p. 1625). His "experience declares it to be unrepresentative": one can only say that he has been very fortunate.

I do not know who Philip Auld is, but he has portrayed most skilfully our disillusion with the N.H.S., increasing with each passing year. In a largely working-class practice in South-West England I, too, can claim to have experienced most of the situations described; as a member of L.M.C. I found that my colleagues were in similar plight. Having left the N.H.S., and the district where I practised, I am able to write without a pseudonym.—I am, etc.,

Helston, Cornwall. CHARLES HAGENBACH.

Gentlemen Boxers' Brains

SIR,—The recent heavy defeat, at the Annual Meeting of the B.M.A., of a motion calling on the Government to declare boxing illegal (*Supplement*, July 2, p. 14) leaves little room for doubt that our profession must include many confirmed amateur pugilists.

Believing as we do, in this department, that any head injury severe enough to cause loss of consciousness is likely to inflict permanent damage on the brain, we are emboldened to ask whether any of these gentlemen boxers would care to further the cause of science by leaving their brains to this department when they die. Intending benefactors may rest assured that any contribution, however small, will be gratefully received.—We are, etc.,

F. B. BYROM.
P. M. DANIEL.

Department of Neuropathology,
Institute of Psychiatry,
The Maudsley Hospital,
Denmark Hill, London, S.E.5.

POINTS FROM LETTERS

Hydroxyzine

Dr. H. MICHAEL BERGER (St. Francis Hospital, Honolulu) writes: It was surprising that your expert contributor failed to mention the anticoagulant potentiating effect of hydroxyzine (April 2, p. 1048). Since myocardial infarction might present a temptation to use anticoagulants and ataractics simultaneously, may I refer to Burrell, Gittinger, and Martinez,[1] who wrote the following? "In some patients who were on anticoagulant therapy concurrently with hydroxyzine, the dosage requirement for the anticoagulant drug was markedly decreased. In some, satisfactory control of anticoagulant therapy could be obtained with about one-half the usual dosage. Patients on combined therapy should be observed closely and prothrombin time checked carefully."

REFERENCE

[1] Burrell, Z. L., Gittinger, W. C., and Martinez, A., *Amer. J. Cardiol.*, 1958, **1**, 624.

Obituary

F. G. GIBBS, F.R.C.S.Ed., F.R.C.P.Ed.
F.D.S. R.C.S.Ed., F.F.A. R.C.S.Eng.

Dr. F. G. Gibbs, lately senior dental surgeon and senior anaesthetist to the Royal Infirmary of Edinburgh, died in Edinburgh on June 24. He was 67 years of age.

Frederick George Gibbs was born in October 11, 1892, and was educated at George Watson's College and in the Edinburgh Medical School, where he qualified in medicine and in dentistry in 1913. After holding resident appointments he served with the R.A.M.C. in France and Italy throughout the first world war. Returning to Edinburgh thereafter, he took the M.R.C.P. of Edinburgh in 1920 and the F.R.C.S. of Edinburgh in 1925, meantime establishing a consultant dental practice which he combined with the practice of anaesthetics. Appointed surgeon to the dental department of the Royal Infirmary in 1927, and anaesthetist in the same year, he served the hospital in this dual capacity for thirty years, holding numerous similar appointments in other hospitals in the city, at the same time continuing his private practice, in which his services as dental consultant and as anaesthetist were in constant demand.

He was elected F.R.C.P.Ed. in 1938, F.D.S. in 1951, and F.F.A. of the Royal College of Surgeons of England in 1954. He was an examiner in dental surgery and in anaesthetics, convener of the Dental Council of the Royal College of Surgeons of Edinburgh, and a member of the General Dental Council until his recent retirement. He was president of the Scottish Society of Anaesthetists in 1955–6.

T. I. W. writes: A man of sincere conviction, Frederick Gibbs served his Kirk as an elder and carried his principles of service in all his ways. Not least was this evident in his relations with his colleagues of whatever rank or age. Throughout his busy professional career he maintained his interest in and enjoyment of the good things in life. As a student he was an athlete and a boxer of note. Later, literature and music were his solace. His recreation was found on golf course and hillside and by the river with rod and fly. Thus he preserved a youthfulness of spirit, so that wherever men met for work or play Freddie was the most welcome among them.

So our sympathy goes to his son and daughter. We too have lost one of our Good Companions.

J. M. CRAIG, M.B., Ch.B., F.R.C.S.

Dr. J. M. Craig, honorary surgeon to the High Wycombe and District War Memorial Hospital, died on May 25 at the age of 65 after many months of painful illness, which he suffered with great fortitude and great understanding.

Joseph Murison Craig's father was a Highland clergyman who married late in life a lady much younger than himself. She presented him with five sons, all to do well in different activities all over the world, from Russia to Malaya. The family was mentioned in many editions of Halliburton's *Handbook of Physiology* because of the age of the father and the excellence of the sons. The mother was naturally left a widow and proceeded to raise her boys to man's estate and independence with little wherewithal, a remarkable feat accomplished by a remarkable woman. "Joe" was the favourite because he was delicate. The Blue Coat School and St. Andrews University provided his education, where in spite of chronic illness and repeated operations he shone in all he did. His poor health spared him service in the first world war, where the other brothers did well. He learnt much of his surgical skill from a wealthy dilettante but very able surgeon and charming man, Mr. Cunning, at the Royal Free Hospital, whose memory he always revered.

St. Mary's Hospital helped him with his Fellowship, which he secured in 1924, but with his poor economic

position he went into general practice in High Wycombe, where he became that often-maligned type, the G.P. surgeon. He was well trained and experienced, and the patients that came his way got as good as anywhere else. Year in, year out, by day or night, he was available, bringing to his emergencies great skill and often remarkable ingenuity. In the work of the general practice he played his part amply and brought to his work much understanding of human psychology, of which he made a great study. In 1948 the Health Service took a lot of joy out of his life and work; his conscience was all the discipline that he needed and he resented any other, but he settled down eventually after a few brushes, because he was consecrated to his work and loved mankind. In High Wycombe and its surroundings he was accorded a love and admiration of which everyone was conscious but himself.

His marriage to a patient, Molly Broom, was the finest thing that happened in his life. Just as his mother stood by him in earlier days, so did his wife in later, and provided a home gay with life and laughter and, true to the Craig tradition, three fine boys who promise well in vocations other than medical. His Highland birth imbued him with a great love of moorland and stream which drew him north whenever opportunity presented. He had a great fund of knowledge of fish and beasties. His last thoughts and talks were on the Highlands, interspersed with long quotations from "Hamewith" and Burns. If I could have set down in his language all his thoughts and experiences there would have been a book which would have equalled those of Barrie.

So, after a dozen or more operations, some of them touch and go, came the last, which failed in its object, and like "Poor Old Joe" in the negro spiritual he heard the gentle voices calling and went, leaving many a sorrowing heart in his profession and his practice.

CHARLES SINGER, M.A., M.D., D.Litt.
Hon.D.Sc., F.R.C.P.

The obituary of Professor Charles Singer was published in the *Journal* of June 18 (p. 1897).

Dr. P. B. POOLE writes from the British Embassy, Warsaw: During the war years the King's School, Canterbury, evacuated to Cornwall only a few miles from Dr. Singer's home. Among his many other commitments in a busy life he undertook to teach practical biology to the sixth form, and we boys visited him once a week by car or bicycle.

In his house he set up a small laboratory with borrowed equipment and specimens. The dogfish and other dissecting specimens he collected locally, often himself. In this room, with a log fire burning, we worked with him, and whilst teaching us the subject in hand he would digress into other topics, inspiring us with his learning and wisdom. His own drawings were superb, and his teaching so clear that we progressed rapidly. He augmented our packed lunches with fruit from his garden, and on special days we had tea in his library. Never once did he complain or report us if we slipped down to the local village for a glass of cider.

To those of us who took up medicine he gave particular encouragement, and not many months passed without a letter from him. Both he and Mrs. Singer were wonderful people to know closely, for it was a friendship which strengthened with the years. There was mutual affection all around in that old house, and a wealth of learning which it was our peculiar privilege to meet then and always remember.

A. R. F. writes: I dissected the brain with Charles Singer when we were students together at St. Mary's—too long ago. Since then I have stayed with him at Oxford, Highgate, and last autumn in Cornwall. Of his high academic distinctions others are much better qualified to speak. I knew, better, the other side of him, his bubbling sense of humour and fondness for reminiscing. Of course, he spent most of a long life in acquiring and dispensing knowledge, but during my visits he cut out Galen, Aristotle, and what not, and I admit to introducing a little flippancy into the conversation. This, I think, may have been a little relief to him. Anyway he seemed to enjoy it for the time being.

I write this simple note to acknowledge with gratitude happy times and kindly hospitality from Professor and Mrs. Singer—Charles and Dorothea. I was glad to hear, from Mrs. Singer, that he passed from sleep to the unknown with no interval of distress. However, I shall miss the visits, chuckles, and recalling of old times. Incidentally, it was a goodish batch that joined St. Mary's at that time or round about then. I am thinking of Singer, Spilsbury, Fleming, Cope, Wilson, Pannett, Juler, Kettle. I write this as an interested also-ran, but with the greatest respect.

Medical Notes in Parliament

WOLFENDEN REPORT STILL IN ADVANCE OF OPINION

TWO-TO-ONE VOTE AGAINST CHANGE IN HOMOSEXUAL LAW

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The Wolfenden recommendation, in Part II of the 1957 Report, that homosexual acts committed in private by consenting adults should cease to be a criminal offence, will not figure in Government legislation during this Parliament. That is the plain inference from the House of Commons vote on June 29, when half the House, 312 of the 630, rejected the idea of early action giving effect to the recommendation by approximately two to one—213 votes to 99 (plus two "tellers" on each side). The division lists showed the distribution of opinion inside the parties: Conservative—173 against, 22 for; Labour—41 against, 75 for; Liberals—4 for; one Independent against.

Government's Duty to Lead

Mr. KENNETH ROBINSON (St. Pancras North, Labour), an Opposition front-bench spokesman on health topics, who moved the motion for early legislation, on this occasion voiced his personal views from a place on the back benches. He said that homosexuality had existed in all societies, from the primitive to the sophisticated; it had been condemned, condoned, and even encouraged at times, but it had never been suppressed. The best estimates were that in Britain to-day about one male in 20 or 25 was an active homosexual, and this was spread fairly evenly through the population. It was largely an involuntary deviation. Some psychiatrists took the view that some types of it were a form of neurosis and could be treated, but the generally accepted view among doctors and sociologists was that this was a disability, a deviation from the norm of the same order as left-handedness and colour-blindness. These unfortunate people deserved their compassion rather than their contempt; yet they chose to brand them indiscriminately as criminals and to isolate them from the community.

The contention that a relaxation of the law in the way proposed would mean that homosexuality would spread like a prairie fire was neither provable nor unprovable. It had not happened in countries where the law had been so relaxed. The Government were entitled to take public opinion into account, but it was frequently the duty of the Government to lead and not follow opinion. If they wanted to make a change there was ample demonstrable public support to justify their action.

Administrative Consequences

Mr. WILLIAM DEEDES (Ashford, Con.) rejected any charge of moral cowardice levelled against the Government merely on the basis that they did not immediately adopt what seemed a right solution to a jurist or sociologist. It was not difficult to reach an intellectual answer to the problem; it was far more difficult to face and work out the administrative consequences of any change. There was the

problem of the universities: if the Wolfenden recommendation was accepted and 21 made the age of consent, for some students homosexuality would be within the law and for others without. There was the problem of the Services, which had profound anxieties; and of the schools. He introduced the issue of moral standards, on which the Home Secretary was to comment later. Leaders of the Church of England had said that this should cease to be the responsibility of the legislators and become that of the upholders of Christian doctrine. It was imperative if the legal restraint were removed that there should be in reach a second line of defence in the medium of moral restraint, and little was being done to build up and strengthen the second line.

The one woman who took part, Mrs. EIRENE WHITE (East Flint, Lab.), objected to the attitude of some men in regarding heterosexual sin as something not as serious as homosexual; and in spite of an avowed abhorrence of homosexual behaviour thought the weight of evidence was on the side of changing the law.

Mr. GODFREY LAGDEN (Hornchurch, Con.) said it was the duty of those in authority to see that good was upheld and evil punished. In his opinion the general run were a dirty-minded danger to the virile manhood of the country.

Dr. A. D. D. BROUGHTON (Batley and Morley, Lab.) said it was not enough to focus attention on the difficulties of a minority group. Their case must be considered, but it was the responsibility of Parliament to legislate for the good of the whole community. The law might be too savage in some cases, but he believed that homosexual practice should remain an offence to show public disapproval of that conduct. The effects of changing it would be harmful and against the public interest.

A Possible Compromise

Mr. WILLIAM SHEPHERD (Cheadle, Con.) said that, although there might be some marginal advantage to homosexuals in an alteration of the law, that would not change the attitude of society to homosexual practices. He introduced the idea of a possible compromise by the repeal of Section 11 of the 1885 Act (the Labouchère amendment). That section made acts of gross indecency illegal and imposed a penalty of two years' imprisonment. To repeal it would mean that acts of gross indecency among consenting adult males in private would not incur the penalty; heterosexual acts of sodomy would continue to do so, and homosexuals would not be able to say they were singled out. Any major alteration of the law would be at this stage wrong.

Mr. DOUGLAS JAY (Battersea, North, Lab.) said there could be no logic or ethic in the distinction between homosexual acts in private and adultery and lesbianism. The House should give the benefit of the doubt on the side of toleration.

Home Secretary's Reply

Mr. R. A. BUTLER said that he had found in the debate a division of opinion equally as great as in 1958. He undertook to examine the complicated issue of repealing the Labouchère amendment, without committing himself further. He had some sympathy with the objective of the proposal that prosecutions should be instituted only by the Director of Public Prosecutions with the assent of the Attorney-General and if the public interest so required—something like that, if it could be reached, might be a solution. But local administration of criminal justice through chief officers of police and the right of the private citizen to prosecute were essential features of the legal system. A very special case must be established before it was departed from and a novelty so untypical introduced into the law. Similarly he rejected the idea of the Home Secretary giving instructions to the police.

This led him to set out some practical questions to which he was still seeking answers. Who would assess the public interest, and how? What did "consenting" mean? Why should the age of consent be 21 for a man and 16 for a girl? Was the Wolfenden exclusion of the Armed Forces—a big omission—to be accepted? How should "in private" be defined? In the discussion of legislation all these would have to be precisely answered.

Current Research on Homosexuality

In an account of the progress that had been made in fulfilment of his promises in the earlier debate he put first the research project by Birkbeck College to compare the psychological and other characteristics of homosexuals sampled from the different groups, and to investigate whether those characteristics differed from group to group and from the characteristics of non-homosexuals. This involved a study of family, social, educational, and occupational backgrounds, and the personal characteristics of those who had been convicted or had been treated in clinics because of such tendencies. Mr. Gordon Westwood, author of *A Minority*, was taking part in this project.

The second line of inquiry was a study not of individual homosexuality but that of groups, and the way in which homosexuals associated with them, with particular reference to the means by which and the extent to which homosexual conduct spread within society. He had also promised investigations on the possibility of influencing homosexual behaviour by psychotherapy or medical means, such as the use of oestrogens. Considerable efforts were being made on this by the Prison Medical Service. It was not possible yet to draw any firm conclusions. He told Mr. Robinson, who questioned him on this point, that this meant that oestrogens were no longer forbidden in prison.

The Law and Morals

After this progress report Mr. Butler came to "the one fundamental question to which we are always brought back." To some people, unfortunately, criminal law and moral law were coterminous; they considered that if conduct was not prohibited by criminal law there was no reason why they should not indulge in it. In a period when religious and ethical restraints were undoubtedly weak, those of the criminal law acquired a special significance. In the present state of crime and morality in the country no one could doubt that the second line of defence mentioned by Mr. Deedes was not sufficiently strong. This was no time to let down the first line.

Would the removal of the legal sanction against homosexual conduct, between consenting adults in private, weaken the moral sanction? Would homosexual conduct spread, or, losing the glamour of rebellion, would it decline? The answers would become less speculative as knowledge grew. Judgment was likely to be sounder if discussion was allowed to proceed and every concrete suggestion examined. He did not believe that the full case for a change had yet been made.

Example of Other Countries

Mr. A. GREENWOOD (Rossendale, Lab.), in an expression of disappointment, summed this up as the promise of every assistance short of actual help.

Mr. E. GARDNER (Billericay, Con.) opposed the motion because of the duty to safeguard youth. Other speakers in the debate included Mr. ROY JENKINS (Birmingham, Stechford, Lab), who wanted early change in the law, and Mr. W. R. REES-DAVIES (Isle of Thanet, Con.), who contested the view that removal of the Labouchère amendment was all the homosexuals wanted. They wanted the elimination of the crimes of sodomy and buggery.

QUESTIONS IN THE COMMONS, JULY 4

Sir Arthur Porritt's Proposals

Mr. WILLIAM GRIFFITHS (Manchester, Exchange, Lab) asked the Minister of Health what recent proposals he had received from the British Medical Association affecting the structure and administration of the National Health Service.

Mr. WALKER-SMITH: I have received no recent proposals from the British Medical Association about the structure and administration of the National Health Service, but I am aware that committees of the Association are considering this matter. I have also seen press reports of what was said at the Association's recent annual conference.

Mr. GRIFFITHS: The Minister will no doubt be hearing from the Association. Sir Arthur Porritt, the President of the Association, described the Health Service as a dismal failure, and suggested that we should end the present system and set up a British medical corporation, and, in particular, end ministerial responsibility to Parliament for the day-to-day conduct of the service.

At a time when most members on both sides of the House want a greater degree of Parliamentary accountability for industries and services, most members would regard it as a retrograde move. Will the Minister give an assurance that the Government will not contemplate a move of any such kind?

Mr. WALKER-SMITH: I have not been asked to. I understand that the presidential orations at the annual conference of the Association do not necessarily reflect the official policy of that Association. I think that the whole House is fully aware of the importance of our constitutional doctrine and the control by Parliament of public money and the consequential responsibility of Ministers therefor.

Medico-Legal

RADIONICS AND THE BLACK BOX

ACTION FOR FRAUD AGAINST MR. DE LA WARR

[FROM A LEGAL CORRESPONDENT]

On June 20, in the Queen's Bench Division of the High Court, Mr. Justice Davies began the hearing of an action by Miss Catherine Olivia Philips, of Four Winds, Porlock, Somerset, against Mr. George Walter de la Warr, of Raleigh Park Road, Oxford, for damages for fraud.

The plaintiff alleges that the defendant is an exponent of, and practitioner in, the pseudo-science of radionics and that in 1956 he fraudulently represented that there were associated with substances, distinctive waves, vibrations, or radiations capable of affecting a device of the defendant called the Delawarr Diagnostic Instrument and capable of being distinguished and positively identified by means of this device, and that the device could be effectively used, with the aid of a spot or specimen of blood from the patient, to diagnose diseases and conditions of the mind and body and the presence of bacteria in the body. Relying on these representations the plaintiff bought a Delawarr Diagnostic Instrument which she alleges did not work and she thereby suffered damage. The defendant denies that he is an exponent of or practitioner in any pseudo-science and pleads that he is a research worker in radionics. He admits that he represented to the plaintiff that the device in the hands of a skilled operator was capable of being affected by radiation from all forms of matter, and that it was a diagnostic instrument, but pleads that those representations were true or that he honestly believed them to be true.

Mr. David Karmel, Q.C., and Mr. D. R. Stuckey appeared for Miss Philips; Mr. Christmas Humphreys, Q.C., Mr. R. J. Trott, and Miss R. Denfield for Mr. de la Warr.

"The Box"

Mr. Karmel said that he would refer to this machine as "the box" and he pointed to a black box, some twenty inches square, which opened on hinges and revealed nine black knobs and dials. This was the box which, it was claimed, could cure people thousands of miles away—a remarkable achievement. Mr. de la Warr had from 1953 occupied himself full-time with "radionics." Miss Philips and her sister became interested in the subject and the sister was the first to visit Mr. de la Warr's laboratories. The sister was given the firm impression that, if only this work would be recognized by the medical authorities, more support would be forthcoming.

Counsel then read from various pamphlets concerning the diagnostic machine in one of which appeared the sentence "it must not be confused with medical diagnosis." Counsel explained that into the cells of the box were put hair or blood from the patient. Usually the cell marked "plus" signified a male and "minus" a female. The box was not connected to anything; it was not plugged in. The dials were set to various numbers, and a sheet of paper representing various parts of the body was placed over a glass, the middle joint of the middle finger was then rubbed along a rubber courser until the finger stuck; that would then be a positive reaction. To prevent getting a false reaction or "stick" there was also a detector switch on the box. Mr. de la Warr told Miss Philips that the only qualification necessary to operate the machine was that she must not be a materialist. Miss Philips became an associate member of the Radionic Association of Great Britain, of which Mr. de la Warr was a founder member and which encouraged the study and use of radionic therapy. She worked at the box without success and eventually gave it up in disgust and despair. She gave it up because she regarded the whole thing as bogus. The whole purpose of this was to cure, although Miss Philips had only reached the stage of diagnosis. Mrs. Margaret Holdsworth, the plaintiff's sister, then gave evidence, and under cross-examination by Mr. Humphreys said that she knew that an essential ingredient in the operation of the instrument was the power of thought.

Plaintiff's Evidence

Miss Philips, the plaintiff, said that she went to Mr. de la Warr's laboratories in 1956 and he told her that the work he was doing was one of the greatest medical and scientific discoveries that had ever been made. As she understood it, the box could diagnose and treat one patient at a time; but a "treatment machine" could broadcast treatment simultaneously to a number of patients. Miss Philips then demonstrated on the box what she had learnt at her second lesson, the diagnostic lesson. The operator obtained a list of the patient's symptoms, set the ninth dial at "ten," concentrated on each symptom in turn, and when a "stick" was obtained, that was the principal symptom; to obtain the principal symptom was the first step; then came location—stomach-ache might be caused by a liver complaint, for example; then detailed location; then detection of cause. Miss Philips said that she continued to practise at the box, but she found out from consulting medical books that the diagnoses she was obtaining were utterly absurd.

Mr. Justice Davies referring to the rate book which listed numbers to be dialled on the box said that some of the diseases in the rate book would never be found in a medical dictionary. For example "happiness and contentment," which struck him as a little odd for a disease. Mr. Humphreys said that was not a disease but a condition.

Tests Refused

Sir Robert Reynolds Macintosh, Nuffield Professor of Anaesthesia at Oxford University, giving evidence for the plaintiff, said that in August, 1953, he was asked by an eminent benefactor to go to the Delawarr laboratories. The witness had warned Mr. de la Warr that some of the blood spots he was going to give him to test would be of healthy children. Mr. de la Warr had replied that the trouble was that his tests might show some malignant disease because the child would develop the disease in the future. He thought that that answer was nonsense and still did. He had also offered to supply Mr. de la Warr with blood from people likely to die within a few days so that his tests could diagnose the causes of death in advance. The tests had been refused. The witness could not get Mr. de la Warr to agree to any tests that would convince him. He came away with the opinion that the whole thing was rubbish. Sir Robert said that Mr. de la Warr had told him that he might detect cancer in an apparently healthy baby, the reason being that it might develop within a few years. In other words predisposition. As to spiritual healing or faith healing the witness did not believe that they could cure organic disease, but it was possible that they could cure mental disease.

Mr. Justice Davies said that it was emphasized by the defendant that the diagnosis capable of being made by the box was not so much of disease but of a tendency to disease. His Lordship chose the venereal diseases as outstanding examples from the rate book. Was it possible by

any means to diagnose a tendency to these diseases if the patients had not got them? The witness replied that in his opinion it was quite impossible. There was no such thing as a predisposition there.

Dr. Hans George Epstein, a specialist in medical physics at the Radcliffe Infirmary, Oxford, said that when he accompanied Sir Robert to the Delawarr laboratories, they were told that the blood spots of patients used in the box, put on to some kind of filter paper, would retain their complete resonance with the living donor for many years. It was made clear to him later when reading some literature that some factor from the human being operating the equipment, mental or thought power or otherwise, was an essential. Dr. Francis Edward Camps, reader in forensic medicine at London University, said that if properly sealed under dry and aseptic conditions blood spots could retain certain of their qualities for many years. But if not treated in this way the results would be quite unpredictable. The witness would call diagnosis from blood spots an element of witch-doctoring.

Dr. Stuart Young, an atomic scientist, said that in the summer of 1956, when he was senior research officer at Oxford University, he spent an afternoon looking over the Delawarr laboratories and the equipment there. He gained the impression that in the absence of any proper tests to show the contrary it was complete nonsense except in so far as patients who were convinced of its usefulness were mentally satisfied. Mr. Edgar A. W. Banner, an electrical engineer, said that the box had no relation to any scientific instrument and that any scientist or engineer would probably regard it as a fake. From the inside it was quite clear that it was not an electrical machine.

Radionic Diagnosis

In his opening speech for the defendant, Mr. Humphreys said that the de la Warrs were pioneers in their field of research and that Mr. de la Warr was an idealistic and perhaps intuitive inventor. It was rarely that a radionic diagnosis could be proved because when diagnosed it was treated on a pre-physical plane and the disease would not show physically. The de la Warrs believed that the instrument functioned above the physical plane and that the factor of thought was not only important but it was seeming to become paramount in diagnosis and treatment with the box. The box was becoming less and less important, save as a focus point for the use of thought. This power was some immense force of the universe itself which seemed to function in a hundred ways—religiously as a blessing, to give messages in telepathy, therapeutically in medicine. What the de la Warrs had been trying to do was to find something in the way of an instrument which would harness this power, whatever it was, and bring it into use for the healing of mankind.

Mr. de la Warr then gave evidence. He said that he resigned his post as assistant to the County Engineer at Oxford in 1953 to concentrate full-time on radionics. The mind was so important in this work that it excluded all physical considerations. They were coming down solidly on the psycho side, but not the psychic side.

Mr. Justice Davies said that, suppose it were conceded that the recognition or diagnosis was on the pre-physical plane, and likewise the treatment, what was the treatment supposed to do? Was it supposed to disperse, for example, gall-stones, or a cancer? Or tend to do so? He did not care how it worked, on whatever plane, but what was the end product? The witness replied that it would tend to cure the cancer or gall-stones physically because the mind and body were so closely related. They had been trying for years to find a way of reconciling this pre-physical state with a physical state. It had been almost impossible even to get the two sides of the bridge to see each other.

Mr. Karmel said that a letter had been received from the defendant's solicitors listing the conditions of a test of the box for the purposes of this action. They were: Mrs. de la Warr must be given a case history, must be given the most outstanding symptom, and one or two others. She would like to take the spot of blood from the patient and she would prefer that the patient should not be aware of the reason. She must work alone on the spot of blood and would prefer that the tests should be on diseases and conditions and not on fractures. The answer would be a radionic diagnosis and not a medical diagnosis. Counsel then asked the defendant if he would be prepared to submit his machine to tests selected by Sir Robert Macintosh and Dr. Camps, consisting of samples of blood taken by an independent party, of a sufficient number to have significant statistical results, the tests being done in the presence of Sir Robert or Dr. Camps.

The witness replied that they were ready to do a radionic diagnosis but would not submit the machine to the tests as laid down. Mr. Justice Davies asked who was to say whether their radionic diagnosis was accurate or not. They might say that a child of six had tuberculosis, but when a doctor said "no," they would say, "He hasn't now, but he will have by the time he is thirty." The witness replied that that was exactly the situation. They were not trying to replace the medical practitioner. They did not claim to work miracles. After the surgeon had done his work they could assist recovery. In 1945 he had told a meeting that he had been able to produce what in fact would cure cancer. The witness thought that he would never make such a statement again after fifteen years' research. The 1945 claim had been withdrawn.

No Claim to Cure on a Physical Plane

Counsel asked if there was any condition of a physical nature which the box would positively cure and the witness replied that they did not claim to cure. Continuing, the witness said that by "personal evocation"—thinking constructively and lovingly—plants could be made to grow better than those which had not been thought of in that way. In general he agreed that the whole of his work was more akin to clairvoyance and telepathy and extra-sensory perception than to anything else. At one stage plants were being treated with an instrument in what was called a typhoon chamber to make them grow faster than other plants. It was a great success, but it showed that the energy was coming from the mind of the operator and that the machine itself was doing very little good.

Mr. Lionel Roy Ogden said that he was an M.A. and a full-time practitioner in Dublin. He always corrected patients who called him "Doctor." He diagnosed with these machines and treated in some other way, usually with homoeopathic remedies and diet. Considering the chronic nature of the cases which came to him he had had very good successes. For the sake of convenience he now used hair for diagnosis instead of blood. His gross income was about £2,000 a year.

Dr. Mary Stevenson said that she was an M.B. and a Ch.B. of Glasgow University, and a D.P.H. of Cambridge University. She practised at Sutton Coldfield, and for ten years she had every day used an instrument similar to the one in this case for diagnosis. It worked and she used it to confirm and sometimes to go beyond what she had been able to find by ordinary methods. One of her patients was not complaining of any pain in the chest, but the diagnostic instrument gave a clue to the fact that there was something in the breast. She medically examined the patient and found in the breast a small nodule and sent her to hospital. The witness later learned that the surgeon had never operated before on such an early cancer.

Mrs. Gertrude Marjorie de la Warr, the defendant's wife, said that she specialized in the treatment of patients rather than the development of machines. She tried to help the people who came to her to get better if she could, but she did not always succeed.

Mr. Justice Davies asked if the witness's evidence about her practice amounted to this: "We cannot cure anything physical. We cannot treat anything physical. But we hope and believe that we can do something in the mental or pre-physical stage that may possibly do the patient good." The witness replied that that was the case and that their work would have an effect on the physical. Mentally better, patients inclined to get physically better.

Healing Through Force Fields

Dr. Griffith Ivor Evans said that his qualifications included M.R.C.S., L.R.C.P., M.D., F.R.C.S. He was a physician who performed his own operations. The black box was an application of Einstein's unified field theory and Eddington's fundamental theory. The operative force was that which gave direction of light. The only name which could be given was energy, the force which passed between two masses and enabled one to affect the other. The field in which Mr. de la Warr was working was a most valuable one. The witness shared Lord Horder's view in this matter that the research ought never to have been allowed to leave the official laboratory in 1924. If Mr. de la Warr claimed that he could detect the sex of a human foetus at two months old it would be an honest mistake. This man did not know enough about wave mechanics to know that you could not do that. The witness worked only in the Ministry of Healing—a branch of the Church which obeyed that part of the Gospel which commanded us to preach the Gospel and heal the sick. The force of prayer was a real force. The witness was not an advocate for this particular box but was an advocate for the principle of healing through the force fields.

Dr. Philip Langton-Lockton, of Langham Place, Northampton, M.R.C.S., L.R.C.P., said that he had taken an interest in radionics since 1957. He had visited the Delawarr laboratories twice, looking at them with a doctor's eye. He had sent patients for the de la Warr treatment and was satisfied with the results. He could only say that the machine worked on a pre-physical level; it might be more correct to say that we just did not know. The witness felt very strongly that it was only our ignorance which prevented us from realizing that all disease was psychologically engendered. Organic disease was only the outcome of years, perhaps, of subconscious conflict and psychological tension. It was somewhere on this level that radionics must work and provide release. Mr. de la Warr was making a very serious attempt to investigate a realm of knowledge about which we know almost nothing.

Miss Joyce Grant Wright, M.R.C.V.S., of Maida Vale, London, said that in 1955 she had been attached to the Putney branch of the R.S.P.C.A. With the consent of the Society and the owners of the animals she selected dogs which had defeated orthodox treatment as cases for de la Warr research. She could recall four cases in which a radionic diagnosis had been correct within medical and scientific limitations. The most impressive case was where a dog was seriously ill and would normally have been operated upon but the owner refused to allow an operation. After radionic treatment the dog recovered.

Dr. Tertius Thomas Boswall Watson, M.B., M.R.C.S., L.R.C.P., of Woldingham, Surrey, said that he had been in general practice but had used homoeopathic remedies. It was nonsense to say that homoeopathy was nonsense. The witness thought that the box enabled the operator to make contact with his unconscious mind and make it function. He must be able to keep his conscious mind in abeyance. By by-passing the conscious mind, the unconscious mind could be used like an electronic computer. The conscious could not accept irrational things as the unconscious mind could, and the box allowed the unconscious mind to work. There was much to be learnt from the arts of the witch doctor and medicine man. The witness had tried to use the box but without success because he had not the capacity.

Mr. Kenneth Macfarlane Walker, F.R.C.S., of Harley Street, W.1, said that he thought that radionics was in line with modern ideas; that everything had lines of thought and put out radiations. He had suggested to the Medical Research Council that they should investigate radionics. From the witness's point of view the defendant's claims were neither ridiculous nor fantastic, but he may have made too many statements and claims that had not been substantiated.

The hearing continues.

Vital Statistics

Registered Disabled Persons

The steady reduction since 1950 in the number of persons on the disabled persons register was maintained during 1959. In October, 1959, there were 695,000 persons registered, compared with 731,000 a year earlier.—Ministry of Labour, *Report of the Year 1959*, H.M.S.O., London.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in May was 85, compared with 70 in the previous month and 74 in May, 1959.

The numbers of cases of industrial diseases in the United Kingdom reported during May were as follows: epitheliomatous ulceration 11, chrome ulceration 22; total 33. There were no deaths.—*Ministry of Labour Gazette*, June, 1960.

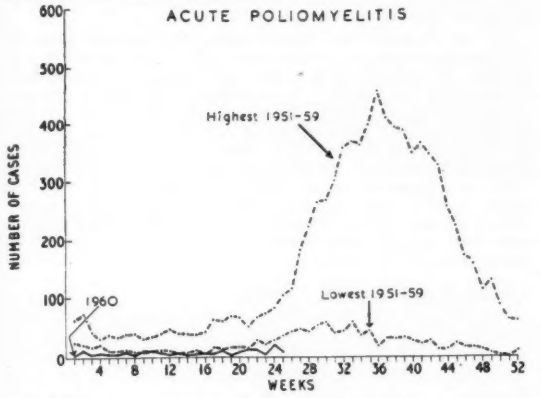
Infectious Diseases

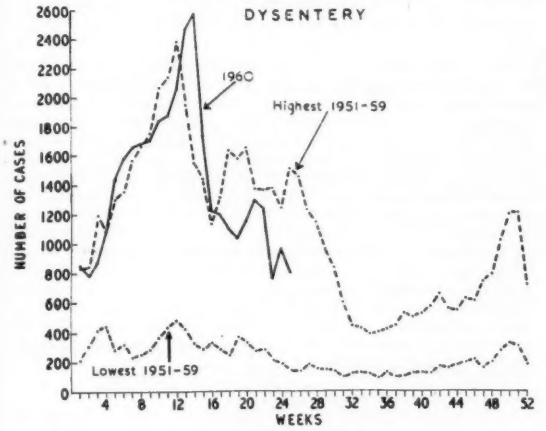
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

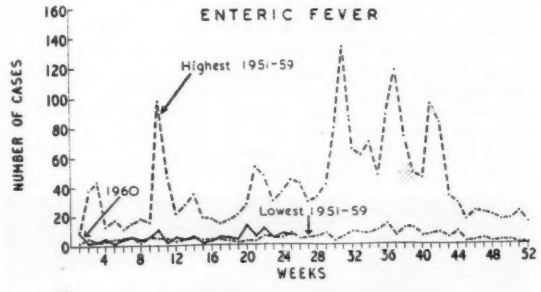
	Week Ending June 18	Week Ending June 25
Dysentery		
Cheshire	23	**24**
Birkenhead C.B.	4	**12**
Dorsetshire	0	**15**
Blandford R.D.	0	**15**
Hampshire	10	**32**
Ringwood and Fordingbridge R.D.	0	**11**
Lancashire	155	**173**
Liverpool C.B.	20	**25**
Manchester C.B.	13	**50**
Morecambe and Heysham M.B.	2	**13**
Urmston U.D.	20	**16**
London	130	**107**
Camberwell	16	**16**
Islington	27	**17**
Norfolk	22	**30**
Northumberland	18	**16**
Newcastle upon Tyne C.B.	13	**12**
Somersetshire	1	**20**
Taunton M.B.	0	**15**
Worcestershire	12	**15**
Worcester C.B.	7	**13**
Yorkshire West Riding	107	**76**
Leeds C.B.	27	**21**
Sheffield C.B.	21	**19**
Glasgow	75	**127**
Food Poisoning		
Kent	6	**38**
Orpington U.D.	4	**18**
Maidstone R.D.	0	**17**
Leicestershire	1	**14**
Leicester C.B.	0	**11**
Lincolnshire	6	**14**
Cleethorpes M.B.	0	**13**
Lancashire	66	**52**
Blackpool C.B.	3	**17**
Cumberland	7	**18**
Millom R.D.	0	**14**
Measles		
Leicestershire	175	**166**
Leicester C.B.	109	**137**
Nottinghamshire	264	**162**
Nottingham C.B.	177	**116**
Lancashire	1,147	**832**
Liverpool C.B.	383	**234**
Manchester C.B.	124	**109**

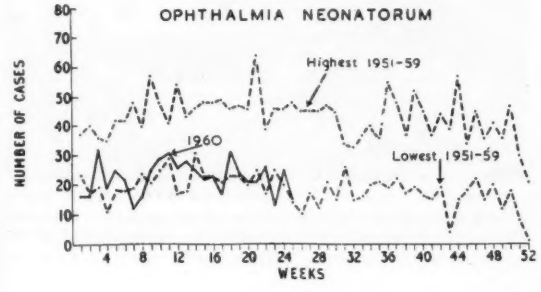
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 18** (No. 24) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	1	1		20	17	2	0	2
Dysentery ..	965	130	129	8	9	878	110	282	19	6
Encephalitis, acute	2	0	1	0		1	0	0	0	
Enteric fever:										
Typhoid ..	0	0	0	0		2	0	0	0	1
Paratyphoid ..	8	1	0	0		3	1	0	0	
Food-poisoning ..	468	34	14	4		298	39	27	0	
Infective enteritis or diarrhoea under 2 years				11	42				5	35
Measles*	2,936	122	53	3	4	10,924	405	242	311	156
Meningococcal infection	17	0	9	0		22	1		0	1
Ophthalmia neonatorum	25	2	6	0		33	7	4	0	
Pneumonia† ..	211	9	126	2	2	160	11	122	12	
Poliomyelitis, acute:										
Paralytic ..	15	3	0	} 0	9	{ 27	11	2	} 2	1
Non-paralytic ..	5	2	0			{ 5	3	1		
Puerperal fever§ ..	173	20	9	3		199	33	1	1	
Scarlet fever ..	346	7	44	12	13	925	72	60	26	14
Tuberculosis:										
Respiratory ..	451	53	82	10		592	70	67	17	
Non-respiratory	65	5	9	2		74	5	14	3	
Whooping-cough ..	1,486	112	235	11	22	658	35	86	42	87

DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	3	1		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	2	0	0	3	0	1	0	1
Influenza	11	0	0	0	0	5	0	0	0	0
Measles		0	0	0	0		0	0	0	
Meningococcal infection		0	1				1	0		
Pneumonia ..	392	24	10	14	2	341	23	15	13	7
Poliomyelitis, acute	0	0		0	2	2	0		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	} 58	{ 5	3	1	3	} 55	{ 4	3	1	3
Non-respiratory		{ 0	1	0	0		{ 0	1	0	3
Whooping-cough ..	0	0	0	0	0	0	0	0	0	1
Deaths 0–1 year ..	296	18	29	7	10	294	30	27	8	17
Deaths (excluding stillbirths) ..	8,740	627	513	142	126	8,273	667	517	99	145
LIVE BIRTHS ..	16,377	1334	1008	289	420	14,670	1219	989	272	331
STILLBIRTHS ..	310	19	29			322	23	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Centenary of St. Peter's Hospital for Stone

On February 11, 1873, a stranger called at St. Peter's Hospital—then in Berners Street—and presented a sealed packet, stipulating that it should not be opened till he had left the building. Inside the packet were ten banknotes of £1,000 each. With this money the new St. Peter's was built in Henrietta Street, Covent Garden, where it was formally opened by H.R.H. PRINCE LEOPOLD, DUKE OF ALBANY, on June 29, 1882. Seventy-eight years later to the day, Prince Leopold's daughter, H.R.H. PRINCESS ALICE, COUNTESS OF ATHLONE, last week unveiled a plaque recording the centenary of the hospital and attended a garden party in the grounds of St. Paul's Church.

Among those presented to her were the dean of the Institute of Urology, Mr. A. R. C. HIGHAM, and the director of studies, Mr. J. D. FERGUSSON, as well as three members of the staff who had served the hospital for many years—a telephonist (26 years' service), a laboratory technician (32 years), and an out-patient nurse (37 years). Mr. A. CLIFFORD MORSON presented Her Royal Highness with an inscribed copy of *St. Peter's Hospital Centenary Book*, which records the history of the hospital and the surgeons connected with it. The hospital's name is said to be the only instance of a saint's name giving an indication of a hospital's special work. The Minister of Health, Mr. D. WALKER-SMITH, attended additional celebrations at the hospital on June 30.

Harveian Society of London

The president of the Harveian Society of London, Mr. TERENCE E. CAWTHORNE, presided at the Buckston Browne/Gray Hill Dinner, which was held at the Zoological Society of London on June 28. The guest of honour, Canon CHARLES E. RAVEN, proposed the toast to the Society, and the president responded. The guests' health was proposed by Dr. C. J. DICKINSON, secretary of the Society, and Lieutenant-General Sir ALEXANDER DRUMMOND replied. After the formal speeches had been completed Mr. W. E. TUCKER was presented by Mr. A. DICKSON WRIGHT with a silver teapot as a mark of appreciation of his services as Treasurer to the Society for the past five years.

British Empire Cancer Campaign

At the annual general meeting on June 29 of the British Empire Cancer Campaign, presided over by H.R.H. the DUKE OF GLOUCESTER, the DUKE OF DEVONSHIRE, the chairman, said that in 1946 the campaign had 11 block grant centres in this country on which £48,295 was spent, while in 1959 the figures were 21 and £595,153, with 450 workers of varying status being supported by campaign funds. The chairman of the Finance Subcommittee, Lord LATHAM, showed in his report that two records had been broken during 1959—the figure of £544,704 from donations and collections, and £281,621 from legacies. Including the investment income, the campaign was well able to meet the year's expenditure of £845,985. The campaign's scientific work is discussed on p. 126 of the *Journal*.

Complaint to Press Council

At a meeting on June 21 the Press Council considered a complaint made on behalf of Professor T. C. GRAY, professor of anaesthetics, Liverpool University, against the *Daily Mail* in respect of its treatment of an article on anaesthesia in the dental chair written by him and published in the *Practitioner*.

In a letter to the Council the Editor of the *Daily Mail* regretted that the two final paragraphs were included in the summary of Professor Gray's article, whereas they were, in fact, written by the newspaper's science correspondent. But he considered that otherwise the *Daily Mail* story was a fair summary of an article which was a matter of public interest. The Press Council decided to issue the following statement: "An article of a highly technical character had been simplified for popular consumption and the Council considers that greater care could have been given to this process. In particular it regrets that the deletion of quotation marks in the editing of the article attributed to the author of the original work statements which were, in fact, those of the science correspondent of the *Daily Mail*. The Council notes, however, that the *Practitioner* courts publicity in the Press by sending advance copies to the newspapers and sometimes drawing particular attention to articles to which it thinks they might make suitable reference."

Chair of Medicine, Charing Cross Hospital Medical School

Dr. H. E. DE WARDENER, reader in medicine at St. Thomas's Hospital Medical School, has been appointed to the University chair of medicine tenable at Charing Cross Hospital Medical School.

Dr. de Wardener, who was educated at Malvern College and St. Thomas's Hospital, qualified M.B., B.S. in 1939, and M.R.C.P. in 1946. He took his M.D. in 1949 and became F.R.C.P. in 1958. He served in the R.A.M.C. from 1939 to 1945, being a prisoner-of-war in Siam from 1942. He was awarded the M.B.E. In 1946 he returned to St. Thomas's as an ex-Service registrar and then spent six months from 1947 to 1948 as registrar at St. Helier Hospital, Carshalton. He returned once more to St. Thomas's in 1948, was appointed senior lecturer in medicine in 1949, and reader in 1959. He undertook research into deficiency diseases during the war and since the war has worked on renal function and renal diseases. His publications have been mainly in the latter field.

Central Health Services Council

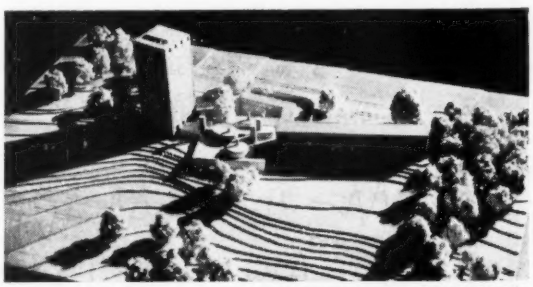
The Central Health Services Council report for 1959 gives details of a subcommittee's report on the prevention of prematurity and the care of the prematurely born. At present perinatal mortality in England and Wales is 35.1 per 1,000 live and stillbirths; if it could be reduced to Sweden's 1955 figure of 28 per 1,000 some 5,000 infant lives would be saved every year.

The report discusses the provision of special baby-care units in each regional hospital area and gives detailed suggestions about accommodation and equipment. The admission to the area specialist centres of all women in labour before the thirty-seventh week, the establishment of an emergency resuscitation team, and improved transport facilities would help to reduce mortality among transported premature infants. Special arrangements for home care, after-care, and follow-up schemes were recommended, and the urgent need for continuing research on the factors causing premature labour was stressed. Among the other topics discussed in the report are an interim report on noise in hospitals, nurses' health records, and the protection of nurses exposed to radiation. Two new committees were set up during the year, one to consider operational research into prescribing and the second to review health education in the National Health Service. (*Report of the Central Health Services Council for the Year Ended December 31, 1959*. H.M.S.O., price 1s. 6d. net.)

Birmingham University Appeal

Birmingham University is making a Diamond Jubilee Appeal for £1½m. towards the cost—£2,588,250—of building seven halls of residence to house 1,480 students by 1965. At present it can only accommodate 460 out of 4,000.

The 45-acre parkland site is within 10 minutes' walk of the main Edgbaston buildings and is attractively timbered. To make the best use of the site some of the buildings are high, and the halls are grouped in pairs, with shared catering and domestic services. Contributions or inquiries should be sent to the Secretary of the University, Edgbaston, Birmingham, 15.



[*Sir Hugh Casson and Neville Conder*

Model of High and Ridge Halls with the proposed re-landscaping. In the centre are the joint dining-rooms, kitchens, and service buildings.

New Hearing-aid Telephone

The Post Office has announced that a new hearing-aid telephone is now available. It is fitted with a small transistorized amplifier fixed in the handset portion of the telephone, with volume controlled by a finger wheel in the earpiece. Additional rental for this new telephone is 15s. a quarter (the same as for the old battery equipment), plus an initial charge of £3 if a colour is chosen. Application should be made to the Telephone Manager, Headquarters Building, St. Martin's-le-Grand, London, E.C.1 (CEN 1170).

Scottish Industrial Rehabilitation

In view of the heavy demands being made on the Hillington Industrial Rehabilitation Unit, the Ministry of Labour in Scotland will increase the number of places at the unit from 100 to 200 from August 8. This will ease the position in the West of Scotland until the Comprehensive Rehabilitation and Assessment Centre at Belvedere Hospital is established in 1963.

Nuclear Safety Advisory Committee

A Nuclear Safety Advisory Committee has been appointed to advise the Minister of Power and the Secretary of State for Scotland on matters relating to safety under the Nuclear Installations (Licensing and Insurance) Act passed last year. Sir ALEXANDER FLECK, F.R.S., is to be chairman. Medical members of the committee include Dr. JOHN LOUTIT, director, Medical Research Council Radiobiological Research Unit, Harwell, and Dr. A. S. MCLEAN, director, Health and Safety Branch, Atomic Energy Authority.

R.S.A. Commonwealth Film Award

The Royal Society of Arts is to make an award—a silver medal and a diploma—to be known as the Royal Society of Arts Commonwealth Film Award, to the film produced in any country of the Commonwealth which is regarded by a panel of judges as having been of greatest service in fostering and promoting progress in either public health or food production in that country. The Central Office of Information, on behalf of the Secretary of State for Commonwealth Relations, is organizing the British entries. Competitors are invited to write to Commonwealth Film Award, Central Office of Information, Hercules Road, London, S.E.1, for details and entry forms. The closing date is August 1.

Grendon Psychiatric Prison

Mr. R. A. BUTLER, the Home Secretary, laid the foundation stone on July 1 of Grendon Psychiatric Prison in Buckinghamshire, the first prison in Great Britain designed for the psychological treatment of crime. He said that those treated, while not certifiably insane or mentally deficient, will be mentally abnormal or disturbed. Treatment may include the use of oestrogens and chemical and biochemical techniques, as well as individual and group psychotherapy. (*The Times*, July 2.)

Emergency Bed Service

"Happy is the country that has no history," says the Emergency Bed Service's annual report up to March 31 this year, commenting on the fact that the year was a remarkably quiet one with 55,847 requests for beds as against 63,807 during the previous year. The service has generally found that a heavy winter is followed by a quieter one. However, during January to March the Medical Referee procedure was resorted to in no less than 11.4% of general cases—a disturbing finding in such a quiet period. The E.B.S. was used slightly less during the year to deal with last-minute admissions of normal maternity cases for social reasons, a practice which had hitherto been increasing and was causing the Service some concern.

People in the News

Dr. W. R. AYKROYD, senior lecturer in the department of human nutrition at the London School of Hygiene and Tropical Medicine, has been made an honorary member of the American Institute of Nutrition. Honorary membership is conferred upon "distinguished individuals of any country who are not members of the Society and who have contributed to the advance of the science of nutrition."

Dr. A. E. MOURANT, director of the Blood Group Reference Laboratory (Medical Research Council), Lister Institute, has been awarded the Huxley Memorial Medal for 1961 of the Royal Anthropological Institute of Great Britain and Ireland.

Dr. N. S. DICKSON has been appointed Assistant Secretary of the British Medical Association to be resident in Northern Ireland. He will be in charge of the Association's Belfast Regional Office. Dr. Dickson qualified in 1931, and has for many years been in general practice. Since 1948 he has served on the Council of the B.M.A. as a representative of the Northern Ireland Branch.

COMING EVENTS

2nd Emily Blake Memorial Lecture: North of England Council, British Empire Cancer Campaign. — Dr. A. GLUCKSMANN (deputy director of Strangeways Research Laboratory, Cambridge): "The Biological Variation and Therapeutic Results in Cancer of the Cervix," July 21, 8 p.m., Royal Victoria Infirmary, Newcastle upon Tyne.

3rd International Conference on Medical Electronics.—Olympia, London, July 21–27, in conjunction with a scientific exhibition. The conference, planned to bring together members of the medical and electrical engineering professions, will be addressed by speakers from many parts of the world, including Spain, Sweden, the U.S.A., and the U.S.S.R., and will cover, among other aspects of the subject, telemetering, applications to space research, aids for the totally deaf and for the blind, automatic control of artificial limbs and of heart action, and instrumentation for obstetric and neonatal research. For details of registration see advertisement p. 57.

St. John's Hospital Dermatological Society.—There will be no meeting of the St. John's Hospital Dermatological Society in July.

British Pharmaceutical Conference.—Newcastle upon Tyne, September 5–9. Details from the Conference Secretariat, 17, Bloomsbury Square, London, W.C.1.

14th Congress of International Scientific Film Association.—Prague, September 16–24, including Festival of Films Presenting Science. Details from the S.F.A., 3, Belgrave Square, London, S.W.1 (BEL 6188).

Pure Food Centenary Conference.—London, September 20–23. Papers include "The Integration of Food Research," by Professor A. C. FRAZER (professor of medical biochemistry and pharmacology, Birmingham University). Details from the Secretariat, Pure Food Centenary, 14, Belgrave Square, London, S.W.1.

Ergonomics in Industry.—D.S.I.R. conference, September 27–29, Connaught Rooms, Great Queen Street, London, W.C.2. Chairman, Sir HAROLD HIMSWORTH, F.R.S. Details from Miss H. M. CLAY, D.S.I.R., 14–18, Cornwall Terrace, Regent's Park, London, N.W.1.

1st British Congress on History of Medicine and Pharmacy.—Organized by the Faculty of the History of Medicine and Pharmacy at the Worshipful Society of Apothecaries of London in co-operation with the Royal Colleges and the Royal Society of Medicine, London, September 29–30. Details from the honorary secretary, Dr. F. N. L. POYNTER, The Wellcome Historical Medical Library, The Wellcome Building, Euston Road, London, N.W.1.

London School of Hygiene and Tropical Medicine.—Course for general practitioners, September 26–October 1. Details on advertisement p. 57.

NEW ISSUES

BRITISH JOURNAL OF PHARMACOLOGY AND CHEMOTHERAPY

The Ganglion-blocking Activity of Aminobicyclo[2,2,1]heptanes (Congeners of Mecamylamine) and Bicyclo[3,2,1]azaoctanes (Bridged Congeners of Pempidine). N. D. Edge, S. J. Corne, G. E. Lee, and W. R. Wragg.
Central Vasomotor Effects of a new Ganglion-blocking Agent—1 : 2 : 2 : 6 : 6-pentamethyl Piperidine (Pempidine). K. N. Dhawan and K. P. Bhargava.
The Inhibition of the Peristaltic Reflex by Substances from Protein Sources. R. Schneider, Hilary Bishop, and B. Shaw.
A Ganglion-stimulating Principle Present in Peptone. W. T. Beraldo and A. Zanotto.
The Absorption of Prothidium by Trypanosoma rhodiense. Angela E. R. Taylor.
The Absorption, Distribution, and Excretion of Prothidium in Rats, Rabbits and Cattle. Angela E. R. Taylor.
The Antimicrobial Properties of Some α-Amino-oxy-acids, α-Amino-oxy-hydrazides, Alkoxyamines, Alkoxydiguanides and Their Derivatives. S. A. Price, P. Mamalis, D. McHale, and J. Green.
Analgesic Action of Ethyl 4-Phenylpiperidine-4-carboxylates with Oxygenated 1-Substitutes. A. M. J. N. Blair and R. P. Stephenson.
Pharmacological Actions of Two New Pethidine Analogues. R. E. Lister.
The Excretion and Stability to Metabolism of Bretylium. W. G. Duncombe and A. McCoubrey.
The Selective Accumulation of Bretylium in Sympathetic Ganglia and Their Postganglionic Nerves. A. L. A. Boura, F. C. Copp, W. G. Duncombe, A. F. Green, and A. McCoubrey.
The Relationship Between the Chemical Structure and Neurotoxicity of Alkyl Organophosphorus Compounds. D. R. Davies, P. Holland, and M. J. Rumens.
A Note on the Demyelination Produced in Hens by Dialkylfluoridates. M. C. Lancaster.
The Influence of Thiopentone Anaesthesia on the Blood Lipid and Blood Sugar Level. J. Fodor and D. Grafnetter.
Apomorphine-induced Pecking in Pigeons. B. N. Dhawan and P. N. Saxena.
The Bronchoconstrictor Action of Bradykinin in the Guinea-pig. H. O. J. Collier, J. A. Holgate, M. Schachter, and Patricia G. Shorley.
Potentiation of Sulphadimidine by 2,4-Diamino-6,7-di-isopropylpteridine and Other 6,7-Disubstituted 2,4-Diaminopteridines Against Eimeria Infections of Chicks. C. Horton-Smith, P. L. Long, and H. O. J. Collier.
The Pharmacology of Chymotrypsin Administered by Inhalation. L. Golberg, L. E. Martin, P. Sheard, and C. Harrison.
Pharmacological Study of a New Antibiotic of Bacillary Origin. Felix Bergmann, R. Reitler, M. Chaimovitz, and David Bergmann.
The Pharmacological Actions of 3-4,Dihydroxyphenyl-α-methylalanine (α-methyldopa), an Inhibitor of 5-Hydroxytryptophan Decarboxylase. S. E. Smith.
Effect of Denervation and of Cocaine on the Action of Sympathomimetic Amines. B. C. R. Strömblad.
Effects of Ergometrine (Ergonovine) on the Isolated Atherosclerotic Heart of the Cholesterol-fed Rabbit. Dorothy Karp, Seymour H. Rinzler, and Janet Travell.
The Effect of Temperature on the Direct Muscle Twitch Response and the Action of Drugs on the Isolated Denervated Rat Diaphragm. E. Letley.
The Effect of Enzyme Inhibitors on Histamine Catabolism in Man. S. E. Lindell, Karen Nilsson, B.-E. Roos, and H. Westling.
Supersensitivity of the Submaxillary Gland Following Exclusion of the Postganglionic Parasympathetic Neurone. N. Emmelin.

Volume 15, No. 2. (Quarterly; £4 4s. annually.)

BRITISH HEART JOURNAL

Endomyocardial Fibrosis in Kenya and Tanganyika Africans. By Peter P. Turner and P. E. C. Manson-Bahr.
The Electrocardiogram in Endomyocardial Fibrosis. By A. W. Williams and K. Somers.
The Electrocardiogram in Subarachnoid Haemorrhage. By Sam Shuster.
Congenital Bicuspid Aortic Valves. By L. G. Bentivoglio, J. Sagarminaga, J. Uricchio, and H. Goldberg.
Congenital Cardiac Malformations in Mongolism. By J. M. Berg, L. Crome and N. E. France.
A B C Leads in Ischaemic Heart Disease. By W. M. Lancaster, T. Semple, and J. C. C. Kelly.
Idiopathic Hyperkinetic State: a New Clinical Syndrome. By Norman Brachfeld and Richard Gorlin.
Immediate and Remote Effects of Resection on the Hypertension in Coarctation of the Aorta. By H. W. March, H. N. Hultgren, and F. Gerbode.
Coronary Arterio-Cameral Fistula. By C. S. Muir.
Drainage Pathways of Pulmonary Veins in Atrial Septal Defect. By E. Braunwald, C. R. Lombardo, and A. G. Morrow.
The Transverse Diameter of the Heart in Older People. By N. R. Cowan.
The Opening Snap in Mitral Incompetence. By P. G. F. Nixon, G. H. Wooler, and L. R. Radigan.
Obstructive Cardiomyopathy Simulating Aortic Stenosis. By J. F. Goodwin, A. Hollman, W. P. Cleland, and D. Teare.
Electrocardiograms of Healthy Men after Strenuous Exercise. By C. A. Rumball and E. D. Acheson.
Sir William Hume. By W. G. A. Swan.
Case Reports
Isolated Laevocardia with Situs Inversus Viscerum. By M. J. T. Fitzgerald.
Laevocardia with Transposition of the Abdominal Viscera. By Maurice Campbell.
Dissecting Aneurysm of the Coronary Artery in Arachnodactyly. By Florence McKeown.
Saccular Dissecting Aneurysm of the Ascending Aorta. By G. H. B. Baker and B. S. L. Kidd.
Iron Incrustation of the Pulmonary Vessels in Patent Ductus Arteriosus with Congenital Mitral Disease. By K. W. Walton and D. Heath.
Primary Pulmonary Hypertension with Obstructive Venous Lesions. By D. B. Brewer and D. R. Humphreys.

Volume XXII, No. 3. (Quarterly; £3 annually.)

BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE

The Human Factor in Shipwrecks and Other Accidents to Ships. A. Otterland and the late B. Roos.
Smoking Habits Related to Injury and Absenteeism in Industry. C. R. Lowe.
Consumption of Medicines on a Working-class Housing Estate. M. Jefferys, J. H. F. Brotherston, and A. Cartwright.
Location of the Adventitious Factors in Haemolytic Disease of the Newborn. G. Knox, S. Murray, and W. Walker.
Premature Birth and Subsequent Admission to Hospital. S. T. Winter and W. Mainzer.
The Families of Dull Children. Z. Stein and M. Susser.
Sickness Absence among Hospital Nurses. A. Barr.

Volume 14, No. 2. (Quarterly; £3 annually.)

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY

Relief of Pain and Paraesthesiae by Nerve Block Distal to a Lesion. R. E. Kibler and P. W. Nathan.
Spasticity and Rigidity: An Experimental Study and Review. Geoffrey Rushworth.
The Effect of Changes in Serum Potassium Upon Myotonia. Peter Leyburn and John N. Walton.
Studies on Intermediate Carbohydrate Metabolism in Multiple Sclerosis. B. McArdle, I. C. K. Mackenzie, and G. R. Webster.
The Surgical Approach to Thoracic Intervertebral Disc Protrusions. Allan Hulme.
Lumbar Disc Protrusions in Pregnancy. J. E. A. O'Connell.
The Influence of a Vascular Factor on the Distribution of Symmetrical Cerebral Calcifications. R. M. Norman and H. Urich.
Ascending Nerve Roots. J. D. Reid.
Abnormality of the Blood-cerebrospinal Fluid Barrier of Patients Suffering from a Depressive Illness. A. J. Coppen.
Adaptation to Postural Change in Psychiatric Patients. A. G. Mezey and P. H. Melville.
The Specificity of Reserpine in the Treatment of Schizophrenia in Identical Twins. S. Benaim.
Malignant Change in an Intracranial Epidermoid. S. I. Davidson and J. M. Small.
Giant Mucocele of the Frontal Sinus. George W. Smith and Marcelino Chavez.
Book Reviews.

Volume 23 (new series), No. 2. (Quarterly; £3 annually.)

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, July 12

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Bertram Louis Abrahams Lecture by Professor Henry Barcroft, F.R.S.: The Nervous Control of the Cutaneous Vessels.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., special lecture by Professor G. D. Robb: The Differential Incidence of Surgical Conditions as Between Maori and White People.

Wednesday, July 13

●GUY'S HOSPITAL MEDICAL SCHOOL.—At Physiology Lecture Theatre, 5 p.m., 14th Addison Lecture by Sir Charles Dodds, F.R.S.: Thomas Addison.
●LONDON HOSPITAL MEDICAL COLLEGE.—At College Hall, Ashfield Street, E., 5.15 p.m., Schorstein Memorial Lecture by Sir Macfarlane Burnet, O.M., F.R.S.: Tissue Transplantations: Potentialities and Limitations. (Tickets from Secretary of College.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.30 p.m., Bernhard Baron Lecture by Professor David Slome: Experimental Research at the Buckston Browne Farm.
ROYAL FREE HOSPITAL, Gray's Inn Road, W.C.—5.15 p.m., Dr. J. R. K. Preedy (Atlanta): Oestrogen Metabolism in Man.

Thursday, July 14

GROUP FOR REPRESENTATION OF THE VIEWS OF CLINICAL PSYCHIATRISTS.—At County Hall, Westminster, S.W. (Principal floor: See notice-board at Belvedere Road entrance), 5.15 p.m., annual general meeting.
LONDON UNIVERSITY.—At St. Thomas's Hospital Medical School, 5.30 p.m., special university lecture in medicine by Professor R. Warren (Harvard): Morphologic Studies of Arteriosclerosis Obliterans.

Friday, July 15

BIOCHEMICAL SOCIETY.—At Department of Physiology, Bristol University, 10.45 a.m., meeting.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Charles Tomes Lecture by Mr. Terence Ward: Surgery of the Mandibular Joint.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Cooper.—On June 11, 1960, at Henley-on-Thames, Walter Edward Cooper, M.R.C.S., L.R.C.P.
Eden.—On June 9, 1960, in hospital at Coventry, Louis Thomas Eden, M.B., Ch.B., of Lime Villa, Wootton Court, Leek Wootton, Warwickshire, formerly of Coventry.
Jones.—On June 6, 1960, Edmund Mervyn Jones, M.R.C.S., L.R.C.P., D.P.H.
Keyms.—On June 12, 1960, at his home, Oyster Haven, St. Mawes, Cornwall, John Johnstone Keyms, L.R.C.P.&S.I. and L.M., L.D.S., late of Richmond, Surrey.
Measham.—On May 24, 1960, John Eric Measham, M.D.
Williams.—On June 4, 1960, at Brisbane, Queensland, Australia, Cyril Henry Williams, M.B., Ch.B., D.T.M.&H., D.P.H., late of Colonial Medical Service, Malaya.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Hypotensive Drugs in Toxaemia

Q.—*What is the place of hypotensive drug therapy in the management and treatment of toxaemia and essential hypertension in pregnancy ?*

A.—The place for hypotensive drugs in the management of the toxaemias of pregnancy is still not finally determined, and the successive discovery of new hypotensives necessitates more and more clinical trials. At present it is probably safe to say that they are most often used in emergency to tide the patient over an acute phase, such as fulminating pre-eclampsia, eclampsia, or sudden aggravation of hypertension, with a view to early induction or caesarean section. There have been many attempts to evaluate the action of hypotensive drugs for the long-term treatment of the toxaemias,[1–5] but, while the reports agree on the symptomatic improvement obtained in the mother, they nearly all caution that the foetal survival rate is little if at all increased thereby, and that careful judgment is still required as to the optimum time for terminating the pregnancy. In chronic hypertensives so treated Dieckmann and Harrod[5] found the incidence of accidental haemorrhage was not decreased. In summary, it might be stated that the use of hypotensive drugs has so far proved much more beneficial to the mother than to the foetus.

REFERENCES

1 de Alvarez, R. R., *Obst. Gynec.*, 1955, **6**, 55.
2 Currens, J. H., Reid, D. E., and Newell, J. L., *J. Amer. med. Ass.*, 1956, **161**, 1232.
3 Bryant, R. D., *Postgrad. Med.*, 1957, **22**, 354.
4 Sellers, A. M., *Amer. J. med. Sci.*, 1957, **233**, 709.
5 Dieckmann, W. J., and Harrod, J. P., *Amer. J. Obstet. Gynec.*, 1958, **76**, 374.

Unequal Breasts

Q.—*A female patient aged 24 shows a marked difference in size between the right and left breasts although she is normal in every other respect. Could any treatment increase the size of the right breast, and is there any possibility of an associated genital infantilism ?*

A.—The breasts, like all paired organs, are rarely exactly equal in size and shape. Even when they appear anatomically similar they often show functional differences. Gross disparity in size is not uncommon and must be regarded as a developmental error. No sort of hormone therapy is of any value in promoting equality in size, and it is unlikely that local massage or other physiotherapy will help. Plastic surgery to increase the size of the smaller breast is not satisfactory, but could be applied to reduce the size of the larger organ. In general, however, this sort of problem is best managed by the wearing of some form of specially padded brassiere.

The embryology of the breast is quite different from that of the gonad and of the genital tract. Genital anomalies are not therefore significantly associated with failure of one breast to develop.

Duration of Immunity after Immunization

Q.—*What is the state of immunity in the case of an ex-Service patient who has had the usual Army course of immunization 10 or 15 years ago but has had no boost since ?*

A.—In such a person there is not likely to be much remaining of the basal immunity to any of the diseases against which he was previously protected except, perhaps, yellow fever. Although the official "life" of a yellow-fever vaccination certificate is only six years, there is some evidence that immunity lasts much longer and perhaps for life. But there would be no satisfactory degree of protection against smallpox, typhoid and paratyphoid, tetanus, or cholera; reinforcing doses of vaccines would be unlikely (except in the case of smallpox) to be sufficient to recall an adequate state of immunity, and full primary courses of inoculations would be indicated.

Vitiligo and the Eyes

Q.—*An Indian woman, aged 60, suffers from vitiligo. The limbs and trunk are extensively involved. Her eyes are blue, and there are brown streaks present. Does this mean that the process of depigmentation affecting the skin may also affect the eyes ?*

A.—Blue eyes with brown streaks are quite common in the Caucasian. I do not know about the Indian. This question would be answered by information about the colour of the eyes before the onset of vitiligo. Has there been any change in eye colour ? I have not myself observed change in eye colour with vitiligo and my ophthalmic colleagues are not familiar with it.

Relieving Symptoms of Hiatus Hernia

Q.—*What are the best medical means for relieving the symptoms of hiatus hernia ?*

A.—Hiatus hernia often leads to reflux oesophagitis, and steps are necessary to minimize reflux by avoiding bending and stooping and by sleeping with two pillows under the shoulders at night. Small meals should be taken rather than one or two big meals.

Southern European Tummy

Q.—*Do you recommend prophylactic chemotherapy (sulphonamides, antibiotics, or both combined) against "southern European tummy" ?*

A.—Prophylactic chemotherapy can be justified only for brief periods under most exceptional circumstances—the operations in jungle warfare in Burma were an example. "Southern European tummy" doubtless is due to a variety of causes, both dietary and infective; not least among the latter are intestinal infections with organisms of the Salmonella and the Shigella groups. Of the latter group, *Sh. sonnei* is the usual pathogen; this organism, as an example, is relatively, and sometimes absolutely, resistant to sulphonamides.

The "normal" intestinal flora of inhabitants of various parts of the world differ with locality. Changes of environment, climate, and diet result in their modification; such modification of itself may well result in a temporary intestinal disturbance. Further changes in the balance of the intestinal flora consequent on prophylactic chemotherapy are hardly likely to help the patient. The entry, about the same time, of lesser pathogens not susceptible to sulphonamides is likely to enhance their effect.

While endeavouring to evade infection by pathogens by taking the usual common-sense precautions, it therefore would seem wiser to defer chemotherapy—sulphonamide or antibiotic—until the need for it is established. An appropriate drug then can be selected for its specific action, and if given in adequate dosage it may be expected to achieve its purpose rapidly and effectively and with the minimum of undesirable side-effects.

Clubbing of Fingers

Q.—*There is often disagreement about what represents definite clubbing of the fingers. Since this is an important sign in respiratory disease, are there any definite and absolute criteria by which one can say whether there is clubbing or not ?*

A.—Like many other signs of disease, clubbing of the fingers develops gradually and may be of various degrees of severity. With the milder degrees of the abnormality it may be impossible to be certain whether clubbing should

be said to be present or not. A change from previously observed normal appearances for the individual patient is probably the earliest indubitable sign.

In clubbed fingers the chief deviations from normal are enlargement of the soft tissues of the finger-ends, which may permit the nail to be rocked longitudinally on its bed; longitudinal and increased transverse curvature of the nails; and obliteration of the normal angle between the base of the nail and the nail fold. In addition, in active clubbing there is hyperaemia of the nail bed, which is particularly evident as redness of the nail fold.

These various aspects of clubbing may not all be present to the same degree, thus giving rise to various types of clubbing. Among these the type named drumstick clubbing has all the features well developed, and particularly the enlargement of the soft tissues; in the so-called parrot-bill clubbing the longitudinal curvature of the nails is the leading feature. In cases of doubt it is usually best simply to describe the abnormality observed and to watch any changes, rather than to insist upon a definite statement that clubbing is or is not present.

Rheumatic Fever

Q.—*A man aged 50 had an attack of rheumatic fever 30 years ago and he now has aortic and mitral stenosis. Should a man of this age have prophylactic penicillin to prevent any further attack, or is the likelihood now so remote as not to be worth the bother?*

A.—Since the likelihood of a second attack of rheumatic fever after this long time and at this age is extremely remote, penicillin prophylaxis is not indicated. It would, however, be a wise precaution to treat any tonsillitis or severe sore throat with a 10-day course of penicillin in bactericidal dosage.

Short-wave Therapy not Carcinogenic

Q.—*Is there any evidence to suggest that short-wave therapy can be a cause of cancer?*

A.—There is no evidence to suggest this. The effect of short-wave diathermy is solely that of heat, and there is no evidence that heat is carcinogenic. But heat is not used if there is any danger of cancer being present, since the increased vascularity produced by heat might accelerate growth.

Pulmonary Embolism and Radical Vulvectomy

Q.—*Are there any statistics available about the liability to pulmonary embolism after radical vulvectomy?*

A.—Surprising though it may seem, those with a large experience of radical vulvectomy operations report a relatively small incidence of post-operative pulmonary embolism. The exact incidence is unknown and must vary from clinic to clinic, and from surgeon to surgeon, according to operative technique and post-operative management. It probably also varies with the community exposed to surgery.

NOTES AND COMMENTS

Snuff-taking.—Dr. GEORGE X. TRIMBLE (California) writes: The answer in the negative by your expert to the question as to whether snuff-taking is harmful ("Any Questions?" April 2, p. 1069) is essentially correct, for there is very little documented in the recent medical literature on the hazards of snuff-taking. However, it might be pointed out that snuff has been reported[1] to be an occasional source of pathogens in chronic pulmonary disease. In the paper I cite as reference, the author, in summarizing his investigation, stated: "It is suggested that snuff be considered a source of pathogens in chronic bronchitis and that its use be proscribed in patients with this disease."

REFERENCE

[1] Dygert, H. P., *New Engl. J. Med.*, 1957, **257**, 311.

OUR EXPERT replies: The paper mentioned by your correspondent refers to a single case. A patient with chronic bronchitis was found to have a persistent growth of *Ps. aeruginosa* in his sputum. This is undoubtedly an unusual organism to be found in these circumstances. In searching for a source for this infection it was found that the patient was a snuff-taker, and *Ps. aeruginosa* was cultured from samples of his snuff. When the patient ceased to use snuff the organism disappeared from his sputum, but it is to be noted that he was also receiving antibiotics at this time. Further investigation showed that other potential pathogenic organisms, including staphylococci, could be obtained on culture from snuff taken from unopened containers. The article also contains interesting information on the preparation of snuff and the extent of its use in the U.S.A. It is recognized that in chronic bronchitis the normal defence mechanisms of the respiratory tract are impaired, and bronchitics are therefore more liable to develop pulmonary infections from pathogenic organisms which enter the upper respiratory tract from the environment. Such organisms are present in dust and other contaminants of the air we breathe, and the additional hazard of taking a little snuff is probably slight. None the less it is one which is avoidable, and the chronic bronchitic who is advised to give up smoking should not turn to snuff as an alternative means of satisfying his craving for nicotine. There is no evidence that persistent snuff-taking will lead to the development of chronic bronchitis or that it is a source of respiratory infection in those who have a healthy respiratory tract.

Birth Risks in Haemophilic Babies.—Dr. F. NOUR-ELDIN (Brentwood) writes: With reference to the question dealing with this subject (May 28, p. 1674), the following may be of interest to readers: A survey which I carried out on 218 cases of haemophilia and Christmas disease revealed that bleeding from the umbilical cord was recorded in four patients only. At first, I thought this might possibly be due to the patients having no definite knowledge of whether or not this early symptom had occurred. However, a further interrogation of 60 mothers of young patients regarding this point confirmed the relative rarity of this type of haemorrhage in these two blood-clotting defects; only three could remember oozing of blood from the navel as being the first manifestation.

Rats in the Sugar.—Mr. J. T. EDWARDS, M.R.C.V.S. (Cheshire), writes: I remember reading in the *Countryman* a few years ago that rats ("Any Questions?" June 4, p. 1752) had successfully been banished from buildings by installing ultraviolet lamps. Rats detest ultraviolet light. I do not remember whether the lamps were left on all night, but probably this would not be necessary, since the rats would soon learn to avoid places where ultraviolet light might shine.

OUR EXPERT replies: It is true that rats dislike bright light, and, given the choice, they will move into the shadows. Ultraviolet light is disliked by rats, but not more so than bright artificial light of any sort. It would seem that the dislike is for brightness of light and not specifically for ultraviolet light. Unfortunately, this information is not helpful in reducing damage by rats, since they will brave the light in order to obtain food. In any event, if a rat repellant could be found, the most it could do would be to persuade rats to go next door. Any improvement in the rat situation must involve the destruction of the rats.

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